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(54) **Platenolide synthase gene**

(57) A DNA molecule isolated from *Streptomyces ambofaciens* encodes the multi-functional proteins which direct the synthesis of the polyketide platenolide.

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Description

The present invention is directed to the DNA isolated from *Streptomyces ambofaciens* responsible for encoding the multi-functional proteins which direct the synthesis of the polyketide platenolide. The present invention also is directed to use of that DNA to produce compounds exhibiting antibiotic activity based on the platenolide structure, including specifically spiramycin and spiramycin analogues and derivatives.

Spiramycin is a macrolide antibiotic useful in both veterinary and human medicine produced by *Streptomyces ambofaciens* (ATCC 15154). Spiramycin is a 16-membered cyclic lactone, platenolide, with three attached sugar residues. Spiramycin's antibiotic activity is believed to be due to its inhibition of protein synthesis by a mechanism that involves binding of the antibiotic to a ribosome. Spiramycin is structurally similar to another antibiotic, tylosin, and the biosynthetic pathways of both are known to be similar.

The biosynthesis of tylosin has been thoroughly investigated (Baltz et al., *Antimicrobial Agents and Chemotherapy,* 20(2):214-225(1981); Beckmann et al., *Genetics and Molecular Biology of Industrial Microorganisms,* (1989):176-186). Polyketides are synthesized via a common mechanistic scheme thought to be related to fatty acid synthesis. The cyclic lactone framework is prepared by a series of condensations involving small carboxylic acid residues. Modifications of the structure, such as ketoreduction, dehydration and enoylreduction, also occur during the processing. The synthesis is driven by a set of large multi-functional polypeptides, referred to as polyketide synthases.

PCT Publication WO 93/13663 describes the organization of the gene encoding the polyketide synthase of *Saccharapolyspora ezythraea.* The gene is organized in modules, with each module effecting one condensation step. The precise sequence of chain growth and the processing of the growing chain is determined by the genetic information in each module. This PCT application describes an approach for synthesizing novel polyketide structures by manipulating in several ways the DNA governing the biosynthesis of the cyclic lactone framework. In order to adapt this methodology to other polyketides, however, the DNA molecules directing the biosynthetic processing must first be isolated.

The present invention is directed to the DNA sequence for the gene cluster responsible for encoding platenolide synthase, the building machinery of platenolide which is the basic building block of spiramycin. As a result, the present invention provides the information needed to synthesize novel spiramycin-related polyketides based on platenolide, arising from modifications of this DNA sequence designed to change the number and type of carboxylic acids incorporated into the growing polyketide chain and to change the kind of post-condensation processing that is conducted.

The present invention provides a DNA molecule comprising an isolated DNA sequence that encodes a platenolide synthase domain. Thus, the present invention provides the DNA molecule of SEQ ID NO:1 and DNA molecules that contain submodules thereof. The present invention also provides the products encoded by said DNA molecules, recombinant DNA expression vectors, and transformed microbial host cells. The present invention is further directed to a method of screening for new antibiotics based on the platenolide structure.

Figure 1 shows the map of the srmG region of the *S. ambofaciens* DNA. Distances in kb are shown relative to the beginning of srmG. Open reading frames (ORF) are indicated by block arrows. The srmG DNA (0-42 kb) is the platenolide PKS region. The indicia Ap, G, E, K, P, and X denote restriction sites ApaI, BglII, EcoRI, KpnI, PstI and XhoI, respectively. Predicted domains for the srmG DNA are labeled as shown. ACP stands for acyl carrier protein; AT stands for acyltransferase; DH stands for dehydratase; ER stands for enoylreductase; KR stands for ketoreductase; KS stands for ketosynthase; and KS' stands for a ketosynthase-like domain in which a glutamine residue is present in the position occupied by an active site cysteine in a normal ketosynthase. KR' is a domain that resembles a ketoreductase but which is predicted to be inactive.

Figure 2 demonstrates the biosynthetic pathway for platenolide synthesis. A denotes malonyl-CoA; B denotes ethylmalonyl-CoA; P denotes methylmalonyl-CoA; C2 denotes a CoA derivative related to malonyl-CoA but of unknown structure.

Figure 3 shows the map of two clones that span the whole region of the srmG DNA.

The term polyketide defines a class of molecules produced through the successive condensation of small carboxylic acids. This diverse group includes plant flavonoids, fungal aflatoxins, and hundreds of compounds of different structures that exhibit antibacterial, antifungal, antitumor, and anthelmintic properties. Some polyketides produced by fungi and bacteria are associated with sporulation or other developmental pathways; others do not yet have an ascribed function. Some polyketides have more than one pharmacological effect. The diversity of polyketide structures reflects the wide variety of their biological properties. Many cyclized polyketides undergo glycosidation at one or more sites, and virtually all are modified during their synthesis through hydroxylation, reduction, epoxidation, etc.

A common feature of compounds in this class is that their synthesis is directed by a complex of multi-functional peptides, termed a "polyketide synthase". Molecular genetic analysis of polyketide synthase genes has revealed two distinct classes of enzymes operating for different polyketides: (a) the aromatics, which are made through an essentially iterative process; (b) the complex polyketides, which comprise several repeats of the same activities arranged in few, very large polypeptides. A common feature among complex polyketide synthase genes is that they are generally arranged in several open reading frames (ORFs), each of which contains one or more repeated units, designated mod-

ules. Each module processes one condensation step and typically requires several activities accomplished by several enzymes including acyl carrier protein (ACP), β-ketosynthase (KS), and acyltransferase (AT).

Therefore a "module" is defined as the genetic element encoding a multi-functional protein segment that is responsible for all of the distinct activities required in a single round of synthesis, i.e., one condensation step and all the β-carbonyl processing steps associated therewith. Each module encodes an ACP, a KS, and an AT activity to accomplish the condensation portion of the synthesis, and selected post-condensation activities to effect β-carbonyl processing. Each module is therefore, further characterized by the inclusion of submodules that are responsible for encoding the distinct activities of a complex polyketide synthase. A "submodule" thus is defined as the portion of the polyketide synthase DNA sequence that encodes a distinct activity, or "domain". A distinct activity or domain is commonly understood to mean that part of the polyketide synthase polyprotein necessary for a given distinct activity.

The protein segments corresponding to each module are called synthase units (SUs). Each SU is responsible for one of the fatty acid-like cycles required for completing the polyketide; it carries the elements required for the condensation process, for selecting the particular extender unit (a coenzyme A thioester of a dicarboxylate) to be incorporated, and for the extent of processing that the β-carbon will undergo. After completion of the cycle, the nascent polyketide is transferred from the ACP it occupies to the KS of the next SU utilized, where the appropriate extender unit and processing level are introduced. This process is repeated, employing a new SU for each elongation cycle, until the programmed length has been reached. As in synthesis of long chain fatty acids, the number of elongation cycles determines the length of the molecule. However, whereas fatty acid synthesis involves a single SU used iteratively, formation of complex polyketides requires participation of a different SU for each cycle, thereby ensuring that the correct molecular structure is produced. The composition of the polyketide synthase gene modules are variable. Some carry the full complement of β-ketoreductase(KR), dehydratase(DH), and enoylreductase(ER) domains, and some encode a particular domain only or lack a functional domain, although much of the sequence is preserved.

This variable composition of the modules, which correlate with the asymmetry in the synthesis of the polyketide precursor, enable a specific step to be assigned to each module. Since each enzymatic activity is involved in a single biochemical step in the pathway, loss of any one activity should affect only a single step in the synthesis. Knowledge of the correlation between the structure of the polyketide and the organization of the polyketide synthase genes enables one to produce altered genes selectively which produce a polyketide derivative with predicted structure.

Because the degree of processing appears to depend on the presence of functional domains in a particular SU, inactivation of a KR, DH, or ER will result in a polyketide less processed at a single site, but only if the altered chain thus produced can be utilized as a substrate for the subsequent synthesis steps. Thus, the inactivation of one of these domains should result in the formation of a polyketide retaining a ketone, hydroxyl, or site of unsaturation at the corresponding position. This rationale has led to the successful production of altered erythromycin derivatives from strains in which a KR or an ER domain had been inactivated.

Thus, one can engineer polyketide pathways by genetic intervention of the polyketide synthase and by adding or eliminating modification steps. Many of the enzymes involved in postpolyketide modifications do not seem to have absolute specificity for a particular structure. In addition one can also select the desired components from a library of polyketide and postpolyketide biosynthesis genes and combine them to produce novel structures.

The present invention provides, in particular, the DNA sequence encoding the polyketide synthase responsible for biosynthesis of platenolide, i.e., platenolide synthase. Platenolide itself is the foundation for spiramycin-related polyketides. The platenolide synthase DNA sequence, which defines the platenolide synthase gene cluster, directs biosynthesis of the platenolide polyketide by encoding the various distinct activities of platenolide synthase.

The gene cluster for platenolide synthase, like other polyketide biosynthetic genes whose organization has been elucidated, is characterized by the presence of several ORFs, each of which contains one or more repeated units termed modules as defined above. Each module also further includes submodules as defined above. Organization of the platenolide synthase gene cluster derived from *Streptomyces ambofaciens* is shown in Figure 1. The accompanying synthetic pathway and the specific carboxylic acid substrates that are used for each condensation reaction and the post-condensation activities of platenolide synthesis are indicated in Figure 2.

A preferred DNA molecule comprising the platenolide synthase gene cluster isolated from *Streptomyces ambofaciens* is represented by SEQ ID NO: 1. Other preferred DNA molecules of the present invention include the various ORFs of SEQ ID NO: 1 that encode individual multi-functional polypeptides. These are represented by ORF1, 350 to 14002, ORF2, 14046 to 20036, ORF3, 20110 to 31284, ORF4, 31329 to 36071, and ORF5, 36155 to 41830 all in SEQ ID NO: 1. The predicted amino acid sequences of the various peptides encoded by these sequences are shown in SEQ ID NO: 2, 3, 4, 5, and 6.

Yet other preferred DNA molecules of the present invention include the modules that encode all the activities necessary for a single round of synthesis. These are represented by starter module 392 to 3424, module 1, 3527 to 8197, module 2, 8270 to 13720, module 3, 14148 to 19730, module 4, 20215 to 24678, module 5, 24742 to 31002, module 6, 31428 to 35837, and module 7, 36257 to 41395 all in SEQ ID NO: 1. The predicted amino acid sequences of the various synthase units encoded by these modules are represented by starter SU 15 to 1025, SU1, 1060 to 2616,

and SU2, 2641 to 4457 in SEQ ID NO: 2; SU3, 35 to 1895 in SEQ ID NO: 3; SU4, 36 to 1523, and SU5, 1545 to 3631 in SEQ ID NO: 4; SU6, 34 to 1503 in SEQ ID NO: 5; SU7, 35 to 1747 all in SEQ ID NO: 6.

Still other preferred DNA molecules include the various submodules that encode the various domains of platenolide synthase. These submodules are represented by KS'(s), 392 to 1603, AT(s), 1922 to 2995, and ACP(s), 3173 to 3424 of starter module in SEQ ID NO:1; KS1, 3527 to 4798, AT1, 5135 to 6208, KR1, 7043 to 7597, and ACP1, 7946 to 8197 of module 1 in SEQ IN NO: 1; KS2, 8270 to 9541, AT2, 9899 to 10909, DH2, 10985 to 11530, KR2, 12596 to 13153, and ACP2, 13469 to 13720 of module 2 in SEQ ID NO: 1; KS3, 14148 to 15422, AT3, 15789 to 16844, DH3, 16914 to 17510, KR3, 18612 to 19166, and ACP3, 19479 to 19730 of module 3 in SEQ ID NO: 1; KS4, 20215 to 21486, AT4, 21889 to 22872, KR'4, 23638 to 24159, and ACP4, 24484 to 24678 of module 4 in SEQ ID NO: 1; KS5, 24742 to 26016, AT5, 26371 to 27381, DH5, 27442 to 27966, ER5, 28843 to 29892, KR5, 29905 to 30462, and ACP5, 30760 to 31002 of module 5 in SEQ ID NP: 1; KS6, 31428 to 32696, AT6, 33024 to 34022, KR6, 34770 to 35327, and ACP6, 35586 to 35837 of module 6 in SEQ ID NO: 1; KS7, 36257 to 37528, AT7, 37898 to 38905, KR7, 39851 to 40408, ACP7, 40658 to 40909, and TE, 41297 to 41395 of module 7 in SEQ ID NO: 1. The predicted amino acid sequences of the various domains encoded by these submodules are represented by KS'(s), 15 to 418, AT(s), 525 to 882, and ACP(s), 942 to 1025 of starter SU in SEQ ID NO:2; KS1, 1060 to 1483, AT1, 1596 to 1953, KR1, 2232 to 2416, and ACP1, 2533 to 2616 of SU1 in SEQ IN NO: 2; KS2, 2641 to 3064, AT2, 3184 to 3520, DH2, 3546 to 3727, KR2, 4083 to 4268, and ACP2, 4374 to 4457 of SU2 in SEQ ID NO: 2; KS3, 35 to 459, AT3, 582 to 933, DH3, 957 to 1155, KR3, 1523 to 1707, and ACP3, 1812 to 1895 of SU3 in SEQ ID NO: 3; KS4, 36 to 459, AT4, 594 to 921, KS^{0}4, 1177 to 1350, and ACP4, 1459 to 1523 of SU4 in SEQ ID NO: 4; KS5, 1545 to 1969, AT5, 2088 to 2424, DH5, 2445 to 2619, ER5, 2912 to 3261, KR5, 3266 to 3451, and ACP5, 3551 to 3631 of SU5 in SEQ ID NO: 4; KS6, 34 to 456, AT6, 566 to 898, KR6, 1148 to 1333, and ACP6, 1420 to 1503 of SU6 in SEQ ID NO: 5; KS7, 35 to 458, AT7, 582 to 917, KR7, 1233 to 1418, ACP7, 1502 to 1585, and TE, 1715 to 1747 of SU7 in SEQ ID NO: 6.

Although not wishing to be bound to any particular technical explanation, a sequence similarity exists among domain boundaries in various polyketide synthase genes. Thus, one skilled in the art is able to predict the domain boundaries of newly discovered polyketide synthase genes based on the sequence information of known polyketide synthase genes. In particular, the boundaries of submodules, domains, and open reading frames in the instant application are predicted based on sequence information disclosed in this application and the locations of the domain boundaries of the erythromycin polyketide synthase (Donadio et al., *GENE*, **111** 51-60 (1992)). Furthermore, the genetic organization of the platenolide synthase gene cluster appears to correspond to the order of the reactions required to complete synthesis of platenolide. This means that the polyketide synthase DNA sequence can be manipulated to generate predictable alterations in the final platenolide product.

The DNA sequence of the platenolide synthase gene can be determined from recombinant DNA clones prepared from the DNA of *Streptomyces ambofaciens*, in particular strain ATCC 15154. The platenolide synthase gene is contained in recombinant DNA vectors pKC1080 and pKC1306 (Figure 1), which are available from the National Center for Agricultural Utilization Research, 1815 North University Street, Peoria, Illinois 61604-3999, in *E. coli* DH10B under accession numbers B-21500 for pKC1080 (deposited Sep 21, 1995) and B-21499 for pKC1306 (deposited Sep 21, 1995) respectively.

Techniques of isolating bacterial DNA are readily available and well known in the art. Any such techniques can be employed in this invention. In particular DNA from these deposited cultures can be isolated as follows. Lyophils of *E. coli* DH10B/pKC1080 or *E. coli* DH10B/pKC1306 are plated onto L-agar (10 g tryptone, 10 g NaCl, 5 g yeast extract, and 15 g agar per liter) plates containing 100 µg/ml apramycin to obtain a single colony isolate of the strain. This colony is used to inoculate about 500 ml of L-broth (10 g tryptone, 10 g NaCl, 5 g yeast extract per liter) containing 100 µg/ml apramycin, and the resulting culture is incubated at 37°C with aeration until the cells reach stationary phase. Cosmid DNA can be obtained from the cells in accordance with procedures known in the art (see e.g., Rao et al., 1987 in Methods in Enzymology, 153:166).

DNA of the current invention can be sequenced using any known techniques in the art such as the dideoxynucleotide chain-termination method (Sanger, et al., Proc. Natl. Acad. Sci. 74:5463 (1977)) with either radioisotopic or fluorescent labels. Double-stranded, supercoiled DNA can be used directly for templates in sequence reactions with sequence-specific oligonucleotide primers. Alternatively, fragments can be used to prepare libraries of either random, overlapping sequences in the bacteriophage M13 or nested, overlapping deletions in a plasmid vector. Individual recombinant DNA subclones are then sequenced with vector-specific oligonucleotide primers. Radioactive reaction products are electrophoresed on denaturing polyacrylamide gels and analyzed by autoradiography. Fluorescently labeled reaction products are electrophoresed and analyzed on Applied Biosystems (ABI Division, Perkin Elmer, Foster City, CA 94404) model 370A and 373A or Dupont (Wilmington, DE) Genesis DNA sequencers. Sequence data are assembled and edited using Genetic Center Group (GCG, Madison, WI) programs GelAssemble and Seqed or the ABI model 670 Inherit Sequence Analysis system and the AutoAssembler and SeqEd programs.

Polypeptides corresponding to a domain, a submodule, a module, a synthesis unit (SU), or an open reading frame can be produced by transforming a host cell such as bacteria, yeast, or eukaryotic cell-expression system with the

cDNA sequence in a recombinant DNA vector. It is well within one skilled in the art to choose among host cells and numerous recombinant DNA expression vectors to practice the instant invention. Multifunctional polypeptides of polyketide platenolide synthase can be extracted from platenolide-producing bacteria such as *Streptomyces ambofaciens* or translated in a cell-free in vitro translation system. In addition, the techniques of synthetic chemistry can be employed to synthesize some of the polypeptides mentioned above.

Procedures and techniques for isolation and purification of proteins produced in recombinant host cells are known in the art. See, for example, Roberts et al., Eur. J. Biochem. 214, 305-311, (1993) and Caffrey et al., FEBS 304, 225-228 (1992) for detailed description of polyketide synthase purification in bacteria. To achieve a homogeneous preparation of a polypeptide, proteins in the crude cell extract can be separated by size and/or charge through different columns well known in the art once or several times. In particular the crude cell extract can be applied to various cellulose columns commercially available such as DEAE-cellulose columns. Subsequently the bound proteins can be eluted and the fractions can be tested for the presence of the polyketide platenolide synthase or engineered derivative protein. Techniques for detecting the target protein are readily available in the art. Any such techniques can be employed for this invention. In particular the fractions can be analysized on Western blot using antibodies raised against a portion or portions of such polyketide platenolide synthase proteins. The fractions containing the polyketide platenolide synthase protein can be pooled and further purified by passing through more columns well known in the art such as applying the pooled fractions to a gel filtration column. When visualized on SDS-PAGE gels homogeneous preparations contain a single band and are substantially free of other proteins.

Knowledge of the platenolide synthase DNA sequence, its genetic organization, and the activities associated with particular open reading frames, modules, and submodules of the gene enables production of novel polyketides having a predicted structure that are not otherwise available. Modifications may be made to the DNA sequence that either alter the initial carboxylic acid building block used or alter the building block added at any of the condensation steps. The platenolide synthase gene may also be modified to alter the actual number of condensation steps done, thereby changing the size of the carbon backbone. Submodules that are part of the present invention may be selectively inactivated thereby giving rise to predictable, novel polyketide structures. Modifications to portions of the DNA sequence that encode the post-condensation processing activities will alter the functional groups appearing at the various condensation sites on the carbon chain backbone.

One skilled in the art is fully familiar with the degeneracy of the genetic code. Consequently, the skilled artisan can modify the specific DNA sequences provided by this disclosure to provide proteins having the same or improved characteristics compared to those polypeptides specifically provided herein. Also, one skilled in the art can modify the DNA sequences to express an identical protein to those provided, albeit expressed at higher levels. Furthermore, one skilled in the art is familiar with means to prepare synthetically, either partially, or in whole, DNA sequences which would be useful in preparing recombinant DNA vectors or coding sequences which are encompassed by the current invention. Additionally, recombinant means for modifying the DNA sequences provided may include for example site-directed deletion or site-directed mutagenesis. These techniques are well known to those skilled in the art and require no further elaboration here. Consequently, as used herein, DNA which is isolated from natural sources, prepared synthetically or semi-synthetically, or which are modified by recombinant DNA methods, are within the scope of the present invention.

Likewise, those skilled in the art will recognize that the polypeptides of the invention may be expressed recombinantly. Alternatively, these polypeptides may be synthesized as well, either in whole or in part, by conventional known non-recombinant techniques; for example, solid-phase synthesis. Thus, the present invention should not be construed as necessarily limited to any specific vector constructions or means for production of the specific polyketide synthase molecules exemplified. These alternate means for preparing the present polypeptides are meant to be encompassed by the present invention.

Many cyclized polyketides undergo glycosidation at one or more sites. Spiramycin is a 16-membered cyclic lactone, platenolide, with three attached sugar residues. The process of converting platenolide to spiramycin is well known in the art. The present invention also provides the information needed to synthesize novel spiramycin-related polyketides based on platenolide. The principles have already been described above. In addition, any product resulting from post-transcriptional or post-translational modification in vivo or in vitro based on the DNA sequence information disclosed here are meant to be encompassed by the present invention.

The following example is provided for exemplification purposes only and is not intended to limit the scope of the invention which has been described in broad terms above.

Example 1:

Specific experimental details and results from the sequencing of platenolide synthase.

The DNA sequence of the *S. ambofaciens* platenolide synthase (srmG) gene can be obtained by sequencing inserts of recombinant DNA subclones containing contiguous or overlapping DNA segments of the region indicated in

Figure 3. All sequences representing srmG are fully contained in the overlapping cosmid clones pKC1080 and pKC1306 (Figure 3). The sequence can be obtained by subcloning and sequencing the fragments bounded by NruI sites at position 1, 0.3 kb, 8.2 kb, 14.1 kb, 20.2 kb, 29.5 kb, 31.4 kb, 41.1 kb and 42.0 kb. In order to obtain the srmG region on a single fragment, the 25.0 kb fragment bounded by the NruI site at position 1 and the SfuI site at 25.0 kb should be isolated from a partial digestion of pKC1080 with restriction enzymes NruI and SfuI. The 17.8 kb DNA fragment bounded by the SfuI sites at 25.0 kb and 42.8 kb should be isolated from a digestion of pKC1306 with the restriction enzyme SfuI. The resulting fragments should be ligated and cloned in an appropriate recombinant DNA vector. Clones containing the correct orientation of the two ligated fragments can be identified by restriction enzyme site mapping.

The principles, preferred embodiments and modes of operation of the present invention have been described in the foregoing specification. The invention which is intended to be protected herein, however, is not to be construed as limited to the particular forms disclosed, since they are to be regarded as illustrative rather than restrictive. Variations and changes may be made by those skilled in the art without departing from the spirit of the invention.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: ELI LILLY AND COMPANY
(B) STREET: Lilly Corporate Center
(C) CITY: Indianapolis
(D) STATE: Indiana
(E) COUNTRY: United States of America
(F) ZIP: 46285

(ii) TITLE OF INVENTION: PLATENOLIDE SYNTHASE GENE

(iii) NUMBER OF SEQUENCES: 6

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: K. G. Tapping
(B) STREET: Erl Wood Manor
(C) CITY: Windlesham
(D) STATE: Surrey
(E) COUNTRY: United Kingdom
(F) ZIP: GU20 6PH

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: Macintosh
(C) OPERATING SYSTEM: Macintosh 7.0
(D) SOFTWARE: Microsoft Word 5.1

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 44377 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 350..14002

(ix) FEATURE:
(A) NAME/KEY: CDS

(B) LOCATION: 14046..20036

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(B) LOCATION: 20110..31284

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(B) LOCATION: 31329..36071

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(B) LOCATION: 36155..41830

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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TGCTGCCGGG AGGGTGTCTG GGGGTGTGCG GTCCGGGCGG GCTGTGCCGG GTGGGGTGGG 1920

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GGGTGGGGTG TTTGCGGAGG TGCTGGATGA GGTGTTGTCG ATGGTGGGGG AGGTGGATGG 2040

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(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4550 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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Val Ala Val Val Gly Met Ala Cys Arg Phe Pro Gly Ala Pro Gly Ile
20 25 30

Ala Glu Phe Trp Lys Leu Leu Thr Asp Gly Arg Asp Ala Ile Gly Arg
35 40 45

Asp Ala Asp Gly Arg Arg Arg Gly Met Ile Glu Ala Pro Gly Asp Phe
50 55 60

Asp Ala Ala Phe Phe Gly Met Ser Pro Arg Glu Ala Ala Glu Thr Asp
65 70 75 80

Pro Gln Gln Arg Leu Met Leu Glu Leu Gly Trp Glu Ala Leu Glu Asp
85 90 95

Ala Gly Ile Val Pro Gly Ser Leu Arg Gly Glu Ala Val Gly Val Phe
100 105 110

Val Gly Ala Met His Asp Asp Tyr Ala Thr Leu Leu His Arg Ala Gly
115 120 125

Ala Pro Val Gly Pro His Thr Ala Thr Gly Leu Gln Arg Ala Met Leu
130 135 140

Ala Asn Arg Leu Ser Tyr Val Leu Gly Thr Arg Gly Pro Ser Leu Ala
145 150 155 160

Val Asp Thr Ala Gln Ser Ser Ser Leu Val Ala Val Ala Leu Ala Val
165 170 175

Glu Ser Leu Arg Ala Gly Thr Ser Arg Val Ala Val Ala Gly Gly Val
180 185 190

Asn Leu Val Leu Ala Asp Glu Gly Thr Ala Ala Met Glu Arg Leu Gly
195 200 205

Ala Leu Ser Pro Asp Gly Arg Cys His Thr Phe Asp Ala Arg Ala Asn
210 215 220

Gly Tyr Val Arg Gly Glu Gly Gly Ala Ala Val Val Leu Lys Pro Leu
225 230 235 240

Ala Asp Ala Leu Ala Asp Gly Asp Pro Val Tyr Cys Val Val Arg Gly
245 250 255

Val Ala Val Gly Asn Asp Gly Gly Gly Pro Gly Leu Thr Ala Pro Asp
260 265 270

Arg Glu Gly Gln Glu Ala Val Leu Arg Ala Ala Cys Ala Gln Ala Arg
275 280 285

Val Asp Pro Ala Glu Val Arg Phe Val Glu Leu His Gly Thr Gly Thr
290 295 300

Pro Val Gly Asp Pro Val Glu Ala His Ala Leu Gly Ala Val His Gly
305 310 315 320

Ser Gly Arg Pro Ala Asp Asp Pro Leu Leu Val Gly Ser Val Lys Thr
325 330 335

Asn Ile Gly His Leu Glu Gly Ala Ala Gly Ile Ala Gly Leu Val Lys
340 345 350

Ala Ala Leu Cys Leu Arg Glu Arg Thr Leu Pro Gly Ser Leu Asn Phe
355 360 365

Ala Thr Pro Ser Pro Ala Ile Pro Leu Asp Gln Leu Arg Leu Lys Val
370 375 380

Gln Thr Ala Ala Ala Glu Leu Pro Leu Ala Pro Gly Gly Ala Pro Leu
385 390 395 400

Leu Ala Gly Val Ser Ser Phe Gly Ile Gly Gly Thr Asn Cys His Val
405 410 415

Val Leu Glu His Leu Pro Ser Arg Pro Thr Pro Ala Val Ser Val Ala
420 425 430

Ala Ser Leu Pro Asp Val Pro Pro Leu Leu Leu Ser Ala Arg Ser Glu
435 440 445

Gly Ala Leu Arg Ala Gln Ala Val Arg Leu Gly Glu Tyr Val Glu Arg
    450   455   460

Val Gly Ala Asp Pro Arg Asp Val Ala Tyr Ser Leu Ala Ser Thr Arg
465   470   475   480

Thr Leu Phe Glu His Arg Ala Val Val Pro Cys Gly Gly Arg Gly Glu
                485   490   495
Leu Val Ala Ala Leu Gly Gly Phe Ala Ala Gly Arg Val Ser Gly Gly
            500   505   510

Val Arg Ser Gly Arg Ala Val Pro Gly Gly Val Gly Val Leu Phe Thr
        515   520   525

Gly Gln Gly Ala Gln Trp Val Gly Met Gly Arg Gly Leu Tyr Ala Gly
    530   535   540

Gly Gly Val Phe Ala Glu Val Leu Asp Glu Val Leu Ser Met Val Gly
545   550   555   560

Glu Val Asp Gly Arg Ser Leu Arg Asp Val Met Phe Gly Asp Val Asp
                565   570   575

Val Asp Ala Gly Ala Gly Ala Asp Ala Gly Ala Gly Ala Gly Ala Gly
            580   585   590

Val Gly Ser Gly Ser Gly Ser Val Gly Gly Leu Leu Gly Arg Thr Glu
        595   600   605

Phe Ala Gln Pro Ala Leu Phe Ala Leu Glu Val Ala Leu Phe Arg Ala
    610   615   620

Leu Glu Ala Arg Gly Val Glu Val Ser Val Val Leu Gly His Ser Val
625   630   635   640

Gly Glu Val Ala Ala Ala Tyr Val Ala Gly Val Leu Ser Leu Gly Asp
                645   650   655

Ala Val Arg Leu Val Val Ala Arg Gly Gly Leu Met Gly Gly Leu Pro
            660   665   670

Val Gly Gly Gly Met Trp Ser Val Gly Ala Ser Glu Ser Val Val Arg
        675   680   685

Gly Val Val Glu Gly Leu Gly Glu Trp Val Ser Val Ala Ala Val Asn
    690   695   700

Gly Pro Arg Ser Val Val Leu Ser Gly Asp Val Gly Val Leu Glu Ser
705   710   715   720

Val Val Ala Ser Leu Met Gly Asp Gly Val Glu Cys Arg Arg Leu Asp
                725   730   735

Val Ser His Gly Phe His Ser Val Leu Met Glu Pro Val Leu Gly Glu
            740   745   750

Phe Arg Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val Arg Pro Gly
        755   760   765

Val Val Val Val Ser Gly Val Ser Gly Gly Val Val Gly Ser Gly Glu
770 775 780

Leu Gly Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu Ala Val Arg
785 790 795 800

Phe Ala Asp Gly Val Gly Val Val Arg Gly Leu Gly Val Gly Thr Leu
805 810 815

Val Glu Val Gly Pro His Gly Val Leu Thr Gly Met Ala Gly Glu Cys
820 825 830

Leu Gly Ala Gly Asp Asp Val Val Val Val Pro Ala Met Arg Arg Gly
835 840 845

Arg Ala Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr Val Phe Thr
850 855 860

Arg Asp Ala Gly Leu Asp Ala Thr Ala Leu His Thr Gly Ser Thr Gly
865 870 875 880

Arg Arg Ile Asp Leu Pro Thr Tyr Pro Phe Gln Arg Arg Thr His Trp
885 890 895

Ser Pro Ala Leu Ser Arg Pro Val Thr Ala Asp Ala Gly Ala Gly Val
900 905 910

Thr Ala Thr Asp Ala Val Gly His Ser Val Ser Pro Asp Pro Glu Ser
915 920 925

Thr Glu Gly Thr Ser His Arg Asp Thr Asp Asp Glu Ala Asp Ser Ala
930 935 940

Ser Pro Glu Pro Met Ser Pro Glu Asp Ala Val Arg Leu Val Arg Glu
945 950 955 960

Ser Thr Ala Ala Val Leu Gly His Asp Asp Pro Gly Glu Val Ala Leu
965 970 975

Asp Arg Thr Phe Thr Ser Gln Gly Met Asp Ser Val Thr Ala Val Glu
980 985 990

Leu Cys Asp Leu Leu Lys Gly Ala Ser Gly Leu Pro Leu Ala Ala Thr
995 1000 1005

Leu Val Tyr Asp Leu Pro Thr Pro Arg Ala Val Ala Glu His Ile Val
1010 1015 1020

Glu Ala Ala Gly Gly Pro Lys Asp Ser Val Ala Gly Gly Pro Gly Val
1025 1030 1035 1040

Leu Ser Ser Ala Ala Val Gly Val Ser Asp Ala Arg Gly Gly Ser Arg
1045 1050 1055

Asp Asp Asp Asp Pro Ile Ala Ile Val Gly Val Gly Cys Arg Leu Pro
1060 1065 1070

Gly Gly Val Asp Ser Arg Ala Ala Leu Trp Glu Leu Leu Glu Ser Gly
1075 1080 1085

```
Ala Asp Ala Ile Ser Ser Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp
    1090                1095                1100

Gly Leu Tyr Asp Pro Glu Pro Gly Thr Pro Gly Lys Thr Tyr Val Arg
1105                1110                1115                1120

Glu Gly Gly Phe Leu His Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe
                1125                1130                1135

Gly Ile Ser Pro Arg Glu Ala Thr Ala Met Asp Pro Gln Gln Arg Leu
            1140                1145                1150

Leu Leu Glu Ala Ser Trp Glu Ala Leu Glu Asp Ala Gly Val Leu Pro
        1155                1160                1165

Glu Ser Leu Arg Gly Gly Asp Ala Gly Val Phe Val Gly Ala Thr Ala
    1170                1175                1180

Pro Glu Tyr Gly Pro Arg Leu His Glu Gly Ala Asp Gly Tyr Glu Gly
1185                1190                1195                1200
Tyr Leu Leu Thr Gly Thr Thr Ala Ser Val Ala Ser Gly Arg Ile Ala
                1205                1210                1215

Tyr Thr Leu Gly Thr Gly Gly Pro Ala Leu Thr Val Asp Thr Ala Cys
            1220                1225                1230

Ser Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ala Leu Arg Arg
        1235                1240                1245

Gly Glu Cys Gly Leu Ala Leu Ala Gly Gly Ala Thr Val Met Ser Gly
    1250                1255                1260

Pro Gly Met Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Pro Asp
1265                1270                1275                1280

Gly Arg Cys Met Pro Phe Ser Ala Asp Ala Asp Gly Thr Ala Trp Ser
                1285                1290                1295

Glu Gly Val Ala Val Leu Ala Leu Glu Arg Leu Ser Asp Ala Arg Arg
            1300                1305                1310

Ala Gly His Arg Val Leu Gly Val Val Arg Gly Ser Ala Val Asn Gln
        1315                1320                1325

Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Arg Ser Ala Gln Glu
    1330                1335                1340

Gly Val Ile Arg Ala Ala Leu Ala Asp Ala Gly Leu Ala Pro Gly Asp
1345                1350                1355                1360

Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Ala Leu Gly Asp Pro
                1365                1370                1375

Ile Glu Ala Ser Ala Leu Leu Ala Thr Tyr Gly Arg Glu Arg Val Gly
            1380                1385                1390

Asp Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Val Gly His Thr Gln
        1395                1400                1405
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Ala Ala Ala Gly Ala Ala Gly Val Val Lys Met Leu Leu Ala Leu Glu
1410 1415 1420

His Gly Thr Leu Pro Arg Thr Leu His Ala Asp Arg Pro Ser Thr His
1425 1430 1435 1440

Val Asp Trp Ser Ser Gly Thr Val Ala Leu Leu Ala Glu Ala Arg Arg
1445 1450 1455

Trp Pro Arg Arg Ser Asp Arg Pro Arg Arg Ala Ala Val Ser Ser Phe
1460 1465 1470

Gly Ile Ser Gly Thr Asn Ala His Leu Ile Ile Glu Glu Ala Pro Glu
1475 1480 1485

Trp Val Glu Asp Ile Asp Gly Val Ala Ala Pro Asp Arg Gly Thr Ala
1490 1495 1500

Asp Ala Ala Ala Pro Ser Pro Leu Leu Leu Ser Ala Arg Ser Glu Gly
1505 1510 1515 1520

Ala Leu Arg Ala Gln Ala Val Arg Leu Gly Glu Tyr Val Glu Arg Val
1525 1530 1535

Gly Ala Asp Pro Arg Asp Val Ala Tyr Ser Leu Ala Ser Thr Arg Thr
1540 1545 1550

Leu Phe Glu His Arg Ala Val Val Pro Cys Gly Gly Arg Gly Glu Leu
1555 1560 1565

Val Ala Ala Leu Gly Gly Phe Ala Ala Gly Arg Val Ser Gly Gly Val
1570 1575 1580

Arg Ser Gly Arg Ala Val Pro Gly Gly Val Gly Val Leu Phe Thr Gly
1585 1590 1595 1600

Gln Gly Ala Gln Trp Val Gly Met Gly Arg Gly Leu Tyr Ala Gly Gly
1605 1610 1615

Gly Val Phe Ala Glu Val Leu Asp Glu Val Leu Ser Met Val Gly Glu
1620 1625 1630

Val Asp Gly Arg Ser Leu Arg Asp Val Met Phe Gly Asp Val Asp Val
1635 1640 1645

Asp Ala Gly Ala Gly Ala Asp Ala Gly Ala Gly Ala Gly Ala Gly Val
1650 1655 1660

Gly Ser Gly Ser Gly Ser Val Gly Gly Leu Leu Gly Arg Thr Glu Phe
1665 1670 1675 1680

Ala Gln Pro Ala Leu Phe Ala Leu Glu Val Ala Leu Phe Arg Ala Leu
1685 1690 1695

Glu Ala Arg Gly Val Glu Val Ser Val Val Leu Gly His Ser Val Gly
1700 1705 1710

Glu Val Ala Ala Ala Tyr Val Ala Gly Val Leu Ser Leu Gly Asp Ala
1715 1720 1725

Val Arg Leu Val Val Ala Arg Gly Gly Leu Met Gly Gly Leu Pro Val
1730 1735 1740

Gly Gly Gly Met Trp Ser Val Gly Ala Ser Glu Ser Val Val Arg Gly
1745 1750 1755 1760

Val Val Glu Gly Leu Gly Glu Trp Val Ser Val Ala Ala Val Asn Gly
1765 1770 1775

Pro Arg Ser Val Val Leu Ser Gly Asp Val Gly Val Leu Glu Ser Val
1780 1785 1790

Val Ala Ser Leu Met Gly Asp Gly Val Glu Cys Arg Arg Leu Asp Val
1795 1800 1805

Ser His Gly Phe His Ser Val Leu Met Glu Pro Val Leu Gly Glu Phe
1810 1815 1820

Arg Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val Arg Pro Gly Val
1825 1830 1835 1840

Val Val Val Ser Gly Val Ser Gly Gly.Val Val Gly Ser Gly Glu Leu
1845 1850 1855

Gly Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu Ala Val Arg Phe
1860 1865 1870

Ala Asp Gly Val Gly Val Val Arg Gly Leu Gly Val Gly Thr Leu Val
1875 1880 1885

Glu Val Gly Pro His Gly Val Leu Thr Gly Met Ala Gly Glu Cys Leu
1890 1895 1900
Gly Ala Gly Asp Asp Val Val Val Val Pro Ala Met Arg Arg Gly Arg
1905 1910 1915 1920

Ala Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr Val Phe Thr Arg
1925 1930 1935

Asp Ala Gly Leu Asp Ala Thr Ala Leu His Thr Gly Ser Thr Gly Arg
1940 1945 1950

Arg Ile Asp Leu Pro Thr Tyr Pro Phe Gln Arg Asp Arg Tyr Trp Leu
1955 1960 1965

Asp Pro Val Arg Thr Ala Val Thr Gly Val Glu Pro Ala Gly Ser Pro
1970 1975 1980

Ala Asp Ala Arg Ala Thr Glu Arg Gly Arg Ser Thr Thr Ala Gly Ile
1985 1990 1995 2000

Arg Tyr Arg Val Ala Trp Gln Pro Ala Val Val Asp Arg Gly Asn Pro
2005 2010 2015

Gly Pro Ala Gly His Val Leu Leu Leu Ala Pro Asp Glu Asp Thr Ala
2020 2025 2030

Asp Ser Gly Leu Ala Pro Ala Ile Ala Arg Glu Leu Ala Val Arg Gly
2035 2040 2045

Ala Glu Val His Thr Val Ala Val Pro Val Gly Thr Gly Arg Glu Ala
2050 2055 2060

Ala Gly Asp Leu Leu Arg Ala Ala Gly Asp Gly Ala Ala Arg Ser Thr
2065 2070 2075 2080

Arg Val Leu Trp Leu Ala Pro Ala Glu Pro Asp Ala Ala Asp Ala Val
2085 2090 2095

Ala Leu Val Gln Ala Leu Gly Glu Ala Val Pro Glu Ala Pro Leu Trp
2100 2105 2110

Ile Thr Thr Arg Glu Ala Ala Ala Val Arg Pro Asp Glu Thr Pro Ser
2115 2120 2125

Val Gly Gly Ala Gln Leu Trp Gly Leu Gly Gln Val Ala Ala Leu Glu
2130 2135 2140

Leu Gly Arg Arg Trp Gly Gly Leu Ala Asp Leu Pro Gly Ser Ala Ser
2145 2150 2155 2160

Pro Ala Val Leu Arg Thr Phe Val Gly Ala Leu Leu Ala Gly Gly Glu
2165 2170 2175

Asn Gln Phe Ala Val Arg Pro Ser Gly Val His Val Arg Arg Val Val
2180 2185 2190

Pro Ala Pro Val Pro Val Pro Ala Ser Ala Arg Thr Val Thr Thr Ala
2195 2200 2205

Pro Ala Thr Ala Val Gly Glu Asp Ala Arg Asn Asp Thr Ser Asp Val
2210 2215 2220

Val Val Pro Asp Asp Arg Trp Ser Ser Gly Thr Val Leu Ile Thr Gly
2225 2230 2235 2240

Gly Thr Gly Ala Leu Gly Ala Gln Val Ala Arg Arg Leu Ala Arg Ser
2245 2250 2255

Gly Ala Ala Arg Leu Leu Leu Val Gly Arg Arg Gly Ala Ala Gly Pro
2260 2265 2270

Gly Val Gly Glu Leu Val Glu Glu Leu Thr Ala Leu Gly Ser Glu Val
2275 2280 2285

Ala Val Glu Ala Cys Asp Val Ala Asp Arg Asp Ala Leu Ala Ala Leu
2290 2295 2300

Leu Ala Gly Leu Pro Glu Glu Arg Pro Leu Val Ala Val Leu His Ala
2305 2310 2315 2320

Ala Gly Val Leu Asp Asp Gly Val Leu Asp Ser Leu Thr Ser Asp Arg
2325 2330 2335

Val Asp Ala Val Leu Arg Asp Lys Val Thr Ala Ala Arg His Leu Asp
2340 2345 2350

Glu Leu Thr Ala Asp Leu Pro Leu Asp Ala Phe Val Leu Phe Ser Ser
2355 2360 2365

Ile Val Gly Val Trp Gly Asn Gly Gly Gln Ala Val Tyr Ala Ala Ala
2370 2375 2380

Asn Ala Ala Leu Asp Ala Leu Ala Gln Arg Arg Arg Ala Arg Gly Ala
2385 2390 2395 2400

Arg Ala Ala Ser Ile Ala Trp Gly Pro Trp Ala Gly Ala Gly Met Ala
2405 2410 2415

Ser Gly Thr Ala Ala Lys Ser Phe Glu Arg Asp Gly Val Thr Ala Leu
2420 2425 2430

Asp Pro Glu Arg Ala Leu Asp Val Leu Asp Asp Val Val Gly Ala Gly
2435 2440 2445

Gly Thr Ser Ala Ala Gly Thr His Ala Ala Gly Glu Ser Ser Leu Leu
2450 2455 2460

Val Ala Asp Val Asp Trp Glu Thr Phe Val Gly Arg Ser Val Thr Arg
2465 2470 2475 2480

Arg Thr Trp Ser Leu Phe Asp Gly Val Ser Ala Ala Arg Ser Ala Arg
2485 2490 2495

Ala Gly His Ala Ala Asp Asp Arg Ala Ala Leu Thr Pro Gly Thr Arg
2500 2505 2510

Pro Gly Asp Gly Ala Pro Gly Gly Ser Gly Gln Asp Gly Gly Glu Gly
2515 2520 2525

Arg Pro Trp Leu Ser Val Gly Pro Ser Pro Ala Glu Arg Arg Arg Ala
2530 2535 2540

Leu Leu Thr Leu Val Arg Ser Glu Ala Ala Gly Ile Leu Arg His Ala
2545 2550 2555 2560

Ser Ala Asp Ala Val Asp Pro Glu Leu Ala Phe Arg Ser Ala Gly Phe
2565 2570 2575

Asp Ser Leu Thr Val Leu Glu Leu Arg Asn Arg Leu Thr Ala Ala Thr
2580 2585 2590

Gly Leu Asn Leu Pro Asn Thr Leu Leu Phe Asp His Pro Thr Pro Leu
2595 2600 2605

Ser Leu Ala Ser His Leu His Asp Glu Leu Phe Gly Pro Asp Ser Glu
2610 2615 2620

Ala Glu Pro Ala Ala Ala Ala Pro Thr Pro Val Met Ala Asp Glu Arg
2625 2630 2635 2640

Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly Gly Val
2645 2650 2655

Ala Ser Pro Asp Asp Leu Trp Asp Leu Val Ala Gly Asp Gly His Thr
2660 2665 2670

Leu Ser Pro Phe Pro Ala Asp Arg Gly Trp Asp Val Glu Gly Leu Tyr
2675 2680 2685

Asp Pro Glu Pro Gly Val Pro Gly Lys Ser Tyr Val Arg Glu Gly Gly
2690 2695 2700

Phe Leu Arg Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe Gly Ile Ser
2705 2710 2715 2720

Pro Arg Glu Ala Thr Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu
2725 2730 2735

Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Val Pro Asp Ser Leu
2740 2745 2750

Arg Gly Thr Arg Thr Gly Val Phe Ser Gly Ile Ser Gln Gln Asp Tyr
2755 2760 2765

Ala Thr Gln Leu Gly Asp Ala Ala Asp Thr Tyr Gly Gly His Val Leu
2770 2775 2780

Thr Gly Thr Leu Gly Ser Val Ile Ser Gly Arg Val Ala Tyr Ala Leu
2785 2790 2795 2800

Gly Leu Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser Ser Ser
2805 2810 2815

Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly Glu Cys
2820 2825 2830

Asp Leu Ala Leu Ala Gly Gly Val Thr Val Met Ala Thr Pro Thr Val
2835 2840 2845

Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg Cys
2850 2855 2860

Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala Glu Gly Val
2865 2870 2875 2880

Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His
2885 2890 2895

Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala
2900 2905 2910

Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg Val Ile
2915 2920 2925

Arg Glu Ala Leu Ala Asp Ala Gly Leu Val Pro Ala Asp Val Asp Val
2930 2935 2940

Val Glu Ala His Gly Thr Gly Thr Ala Leu Gly Asp Pro Ile Glu Ala
2945 2950 2955 2960

Gly Ala Leu Leu Ala Thr Tyr Gly Arg Glu Arg Val Gly Asp Pro Leu
2965 2970 2975

Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala
2980 2985 2990

Gly Val Gly Gly Val Ile Lys Val Val Gln Gly Met Arg His Gly Ser
2995 3000 3005

Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ser Lys Val Glu Trp
3010 3015 3020

Ala Ser Gly Ala Val Glu Leu Leu Thr Glu Thr Arg Ser Trp Pro Arg
3025 3030 3035 3040

Arg Val Glu Arg Val Arg Arg Ala Ala Val Ser Ala Phe Gly Val Ser
3045 3050 3055

Gly Thr Asn Ala His Val Val Leu Glu Glu Ala Pro Ala Glu Ala Gly
3060 3065 3070

Ser Glu His Gly Asp Gly Pro Glu Pro Glu Arg Pro Asp Ala Val Thr
3075 3080 3085

Gly Pro Leu Ser Trp Val Leu Ser Ala Arg Ser Glu Gly Ala Leu Arg
3090 3095 3100

Ala Gln Ala Val Arg Leu Arg Glu Cys Val Glu Arg Val Gly Ala Asp
3105 3110 3115 3120

Pro Arg Asp Val Ala Gly Ser Leu Val Val Ser Arg Ala Ser Phe Gly
3125 3130 3135

Glu Arg Ala Val Val Val Gly Arg Gly Arg Glu Glu Leu Leu Ala Gly
3140 3145 3150

Leu Asp Val Val Ala Ala Gly Ala Pro Val Gly Val Ser Ser Gly Ala
3155 3160 3165

Gly Ala Val Val Arg Gly Ser Ala Val Arg Gly Arg Gly Val Gly Val
3170 3175 3180

Leu Phe Thr Gly Gln Gly Ala Gln Trp Val Gly Met Gly Arg Gly Leu
3185 3190 3195 3200

Tyr Ala Gly Gly Gly Val Phe Ala Glu Val Leu Asp Glu Val Leu Ser
3205 3210 3215

Val Val Gly Glu Val Asp Gly Arg Ser Leu Arg Asp Val Met Phe Ala
3220 3225 3230

Asp Ala Asp Ser Val Leu Gly Gly Leu Leu Gly Arg Thr Glu Phe Ala
3235 3240 3245

Gln Pro Ala Leu Phe Ala Leu Glu Val Ala Leu Phe Arg Ala Leu Glu
3250 3255 3260

Ala Arg Gly Val Glu Val Ser Val Val Leu Gly His Ser Val Gly Glu
3265 3270 3275 3280

Val Ala Ala Ala Tyr Val Ala Gly Val Leu Ser Leu Gly Asp Ala Val
3285 3290 3295

Arg Leu Val Val Ala Arg Gly Gly Leu Met Gly Gly Leu Pro Val Gly
3300 3305 3310

Gly Gly Met Trp Ser Val Gly Ala Ser Glu Ser Val Val Arg Gly Val
3315 3320 3325

Val Glu Gly Leu Gly Glu Trp Val Ser Val Ala Ala Val Asn Gly Pro
3330 3335 3340

Arg Ser Val Val Leu Ser Gly Asp Val Gly Val Leu Glu Ser Val Val
3345 3350 3355 3360

Val Thr Leu Met Gly Asp Gly Val Glu Cys Arg Arg Leu Asp Val Ser
3365 3370 3375

His Gly Phe His Ser Val Leu Met Glu Pro Val Leu Gly Glu Phe Arg
3380 3385 3390

Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val Arg Pro Gly Val Val
3395 3400 3405

Val Val Ser Gly Val Ser Gly Gly Val Val Gly Ser Gly Glu Leu Gly
3410 3415 3420

Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu Ala Val Arg Phe Ala
3425 3430 3435 3440

Asp Gly Val Gly Val Val Arg Gly Leu Gly Val Gly Thr Leu Val Glu
3445 3450 3455

Val Gly Pro His Gly Val Leu Thr Gly Met Ala Gly Gln Cys Leu Glu
3460 3465 3470

Ala Gly Asp Asp Val Val Val Val Pro Ala Met Arg Arg Gly Arg Pro
3475 3480 3485

Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr Val Phe Thr Arg Asp
3490 3495 3500

Ala Gly Leu Asp Ala Thr Thr Leu His Thr Gly Ser Thr Gly Arg Arg
3505 3510 3515 3520

Ile Asp Leu Pro Thr Tyr Pro Phe Gln His Asn Arg Tyr Trp Ala Thr
3525 3530 3535

Gly Ser Val Thr Gly Ala Thr Gly Thr Ser Ala Ala Ala Arg Phe Gly
3540 3545 3550

Leu Glu Trp Lys Asp His Pro Phe Leu Ser Gly Ala Thr Pro Ile Ala
3555 3560 3565

Gly Ser Gly Ala Leu Leu Leu Thr Gly Arg Val Gly Leu Ala Ala His
3570 3575 3580

Pro Trp Leu Ala Asp His Ala Ile Ser Gly Thr Val Leu Leu Pro Gly
3585 3590 3595 3600

Thr Ala Ile Ala Asp Leu Leu Leu Arg Ala Val Glu Glu Val Gly Ala
3605 3610 3615

Gly Gly Val Glu Glu Leu Thr Leu His Glu Pro Leu Leu Leu Pro Glu
3620 3625 3630

Arg Gly Gly Leu His Val Gln Val Leu Val Glu Ala Ala Asp Glu Gln
3635 3640 3645

Gly Arg Arg Ala Val Ala Val Ala Ala Arg Pro Glu Gly Pro Gly Arg
3650 3655 3660
Asp Gly Glu Glu Gln Glu Trp Thr Arg His Ala Glu Gly Val Leu Thr
3665 3670 3675 3680

Ser Thr Glu Thr Ala Val Pro Asp Met Gly Trp Ala Ala Gly Ala Trp
3685 3690 3695

Pro Pro Pro Gly Ala Glu Pro Ile Asp Val Glu Glu Leu Tyr Asp Ala
3700 3705 3710

Phe Ala Ala Asp Gly Tyr Gly Tyr Gly Pro Ala Phe Thr Ala Leu Ser
3715 3720 3725

Gly Val Trp Arg Leu Gly Asp Glu Leu Phe Ala Glu Val Arg Arg Pro
3730 3735 3740

Ala Gly Gly Ala Gly Thr Thr Gly Asp Gly Phe Gly Val His Pro Ala
3745 3750 3755 3760

Leu Phe Asp Ala Ala Leu His Pro Trp Arg Ala Gly Gly Leu Leu Pro
3765 3770 3775

Asp Thr Gly Gly Thr Thr Trp Ala Pro Phe Ser Trp Gln Gly Ile Ala
3780 3785 3790

Leu His Thr Thr Gly Ala Glu Thr Leu Arg Val Arg Leu Ala Pro Ala
3795 3800 3805

Ala Gly Gly Thr Glu Ser Ala Phe Ser Val Gln Ala Ala Asp Pro Ala
3810 3815 3820

Gly Thr Pro Val Leu Thr Leu Asp Ala Leu Leu Leu Arg Pro Val Thr
3825 3830 3835 3840

Leu Gly Arg Ala Asp Ala Pro Gln Pro Leu Tyr Arg Val Asp Trp Gln
3845 3850 3855

Pro Val Gly Gln Gly Thr Glu Ala Ser Gly Ala Gln Gly Trp Thr Val
3860 3865 3870

Leu Gly Gln Ala Ala Ala Glu Thr Val Ala Gln Pro Ala Ala His Ala
3875 3880 3885

Asp Leu Thr Ala Leu Arg Thr Ala Val Ala Ala Ala Gly Thr Pro Val
3890 3895 3900

Pro Arg Leu Val Val Val Ser Pro Val Asp Thr Arg Leu Asp Glu Gly
3905 3910 3915 3920

Pro Val Leu Ala Asp Ala Glu Ala Arg Ala Arg Ala Gly Asp Gly Trp
3925 3930 3935

Asp Asp Asp Pro Leu Arg Val Ala Leu Gly Arg Gly Leu Thr Leu Val
3940 3945 3950

Arg Glu Trp Val Glu Asp Glu Arg Leu Ala Asp Ser Arg Leu Val Val
3955 3960 3965

Leu Thr Arg Gly Ala Val Ala Ala Gly Pro Gly Asp Val Pro Asp Leu
3970 3975 3980

Thr Gly Ala Ala Leu Trp Gly Leu Leu Arg Ser Ala Gln Ser Glu Tyr
3985 3990 3995 4000

Pro Asp Arg Phe Thr Leu Ile Asp Val Asp Asp Ser Pro Glu Ser Arg
4005 4010 4015

Ala Ala Leu Pro Arg Ala Leu Gly Ser Ala Glu Arg Gln Leu Ala Leu
4020 4025 4030

Arg Thr Gly Asp Val Leu Ala Pro Ala Leu Val Pro Met Ala Thr Arg
4035 4040 4045

Pro Ala Glu Thr Thr Pro Ala Thr Ala Val Ala Ser Ala Thr Thr Gln
4050 4055 4060

Thr Gln Val Thr Ala Pro Ala Pro Asp Asp Pro Ala Ala Asp Ala Val
4065 4070 4075 4080

Phe Asp Pro Ala Gly Thr Val Leu Ile Thr Gly Gly Thr Gly Ala Leu
4085 4090 4095

Gly Arg Arg Val Ala Ser His Leu Ala Arg Arg Tyr Gly Val Arg His
4100 4105 4110

Met Leu Leu Val Ser Arg Arg Gly Pro Asp Ala Pro Glu Ala Gly Pro
4115 4120 4125

Leu Glu Arg Glu Leu Ala Gly Leu Gly Val Thr Ala Thr Phe Leu Ala
4130 4135 4140

Cys Asp Leu Thr Asp Ile Glu Ala Val Arg Lys Ala Val Ala Ala Val
4145 4150 4155 4160

Pro Ser Asp His Pro Leu Thr Gly Val Val His Thr Ala Gly Val Leu
4165 4170 4175

Asp Asp Gly Ala Leu Thr Gly Leu Thr Arg Gln Arg Leu Asp Thr Val
4180 4185 4190

Leu Arg Pro Lys Ala Asp Ala Val Arg Asn Leu His Glu Ala Thr Leu
4195 4200 4205

Asp Arg Pro Leu Arg Ala Phe Val Leu Phe Ser Ala Ala Ala Gly Leu
4210 4215 4220

Leu Gly Arg Pro Gly Gln Ala Ser Tyr Ala Ala Ala Asn Ala Val Leu
4225 4230 4235 4240

Asp Ala Leu Ala Gly Ala Arg Arg Ala Ala Gly Leu Pro Ala Val Ser
4245 4250 4255

Leu Ala Trp Gly Leu Trp Asp Glu Gln Thr Gly Met Ala Gly Gly Leu
4260 4265 4270

Asp Glu Met Ala Leu Arg Val Leu Arg Arg Asp Gly Ile Ala Ala Met
4275 4280 4285

Pro Pro Glu Gln Gly Leu Glu Leu Leu Asp Leu Ala Leu Thr Gly His
4290 4295 4300

Arg Asp Gly Pro Ala Val Leu Val Pro Leu Leu Leu Asp Gly Ala Ala
4305 4310 4315 4320

Leu Arg Arg Thr Ala Lys Glu Arg Gly Ala Ala Thr Met Ser Pro Leu
4325 4330 4335

Leu Arg Ala Leu Leu Pro Ala Ala Leu Arg Arg Ser Gly Gly Ala Gly
4340 4345 4350

Ala Pro Ala Ala Ala Asp Arg His Gly Lys Glu Ala Asp Pro Gly Ala
4355 4360 4365

Gly Arg Leu Ala Gly Met Val Ala Leu Glu Ala Ala Glu Arg Ser Ala
4370 4375 4380

Ala Val Leu Glu Leu Val Thr Glu Gln Val Ala Glu Val Leu Gly Tyr
4385 4390 4395 4400

Ala Ser Ala Ala Glu Ile Glu Pro Glu Arg Pro Phe Arg Glu Ile Gly
4405 4410 4415

Val Asp Ser Leu Ala Ala Val Glu Leu Arg Asn Arg Leu Ser Arg Leu
4420 4425 4430

Val Gly Leu Arg Leu Pro Thr Thr Leu Ser Phe Asp His Pro Thr Pro
4435 4440 4445

Lys Asp Met Ala Gln His Ile Asp Gly Gln Leu Pro Arg Pro Ala Gly
4450 4455 4460

Ala Ser Pro Ala Asp Ala Ala Leu Glu Gly Ile Gly Asp Leu Ala Arg
4465 4470 4475 4480

Ala Val Ala Leu Leu Gly Thr Gly Asp Ala Arg Arg Ala Glu Val Arg
4485 4490 4495

Glu Gln Leu Val Gly Leu Leu Ala Ala Leu Asp Pro Pro Gly Arg Thr
4500 4505 4510

Gly Thr Ala Ala Pro Gly Val Pro Ser Gly Ala Asp Gly Ala Glu Pro
4515 4520 4525

Thr Val Thr Asp Arg Leu Asp Glu Ala Thr Asp Asp Glu Ile Phe Ala
4530 4535 4540

Phe Leu Asp Glu Gln Leu
4545 4550

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1996 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```
Met Thr Ala Glu Asn Asp Lys Ile Arg Ser Tyr Leu Lys Arg Ala Thr
1               5                   10                  15

Ala Glu Leu His Arg Thr Lys Ser Arg Leu Ala Glu Val Glu Ser Ala
            20                  25                  30

Ser Arg Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly
        35                  40                  45

Gly Val Ala Ser Pro Asp Asp Leu Trp Asp Leu Val Ala Ala Gly Thr
    50                  55                  60

Asp Ala Val Ser Ala Phe Pro Val Asp Arg Gly Trp Asp Val Glu Gly
65                  70                  75                  80
Leu Tyr Asp Pro Asp Pro Glu Ala Val Gly Arg Ser Tyr Val Arg Glu
                85                  90                  95

Gly Gly Phe Leu His Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe Gly
            100                 105                 110

Ile Ser Pro Arg Glu Ala Ala Ala Met Asp Pro Gln Gln Arg Leu Leu
        115                 120                 125

Leu Glu Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Val Pro Ala
    130                 135                 140

Ser Leu Arg Gly Thr Arg Thr Gly Val Phe Thr Gly Val Met Tyr Asp
145                 150                 155                 160

Asp Tyr Gly Ser Arg Phe Asp Ser Ala Pro Pro Glu Tyr Glu Gly Tyr
                165                 170                 175

Leu Val Asn Gly Ser Ala Gly Ser Ile Ala Ser Gly Arg Val Ala Tyr
            180                 185                 190

Ala Leu Gly Leu Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser
        195                 200                 205

Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly
    210                 215                 220

Glu Cys Asp Leu Ala Leu Ala Gly Gly Val Thr Val Met Ala Thr Pro
225                 230                 235                 240

Thr Val Leu Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly
                245                 250                 255

Arg Cys Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala Glu
            260                 265                 270

Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn
        275                 280                 285

Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp
```

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        290                 295                 300

Gly Ala Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg
305                 310                 315                 320

Val Ile Arg Glu Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp Val
                325                 330                 335

Asp Ala Val Glu Ala His Gly Thr Gly Thr Pro Leu Gly Asp Pro Ile
            340                 345                 350

Glu Ala Gly Ala Leu Leu Ala Thr Tyr Gly Ser Glu Arg Gln Gly Gln
        355                 360                 365

Gly Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln
    370                 375                 380

Ala Ala Ala Gly Val Gly Gly Val Ile Lys Val Val Gln Ala Met Arg
385                 390                 395                 400

His Gly Ser Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ser Lys
                405                 410                 415

Val Glu Trp Ala Ser Gly Ala Val Glu Leu Leu Thr Glu Thr Arg Ser
            420                 425                 430
Trp Pro Arg Arg Val Glu Arg Val Arg Arg Ala Ala Val Ser Ala Phe
        435                 440                 445

Gly Val Ser Gly Thr Asn Ala His Val Val Leu Glu Glu Ala Pro Ala
    450                 455                 460

Glu Ala Gly Ser Glu His Gly Asp Gly Pro Glu Pro Glu Arg Pro Asp
465                 470                 475                 480

Ala Val Thr Gly Pro Leu Ser Trp Val Leu Ser Ala Arg Ser Glu Gly
                485                 490                 495

Ala Leu Arg Ala Gln Ala Val Arg Leu Arg Glu Cys Val Glu Arg Val
            500                 505                 510

Gly Ala Asp Pro Arg Asp Val Ala Gly Ser Leu Val Val Ser Arg Ala
        515                 520                 525

Ser Phe Gly Glu Arg Ala Val Val Val Gly Arg Gly Arg Glu Glu Leu
    530                 535                 540

Leu Ala Gly Leu Asp Val Val Ala Ala Gly Ala Pro Val Gly Val Ser
545                 550                 555                 560

Gly Gly Val Ser Ser Gly Ala Gly Ala Val Val Arg Gly Ser Ala Val
                565                 570                 575

Arg Gly Arg Gly Val Gly Val Leu Phe Thr Gly Gln Gly Ala Gln Trp
            580                 585                 590

Val Gly Met Gly Arg Gly Leu Tyr Ala Gly Gly Gly Val Phe Ala Glu
        595                 600                 605

Val Leu Asp Glu Val Leu Ser Val Val Gly Glu Val Gly Gly Trp Ser
```

610 615 620

Leu Arg Asp Val Met Phe Gly Asp Val Asp Val Asp Ala Gly Ala Gly
625 630 635 640

Ala Asp Ala Gly Val Gly Ser Gly Val Gly Val Gly Gly Leu Leu Gly
645 650 655

Arg Thr Glu Phe Ala Gln Pro Ala Leu Phe Ala Leu Glu Val Ala Leu
660 665 670

Phe Arg Ala Leu Glu Ala Arg Gly Val Glu Val Ser Val Val Leu Gly
675 680 685

His Ser Val Gly Glu Val Ala Ala Ala Tyr Val Ala Gly Val Leu Ser
690 695 700

Leu Gly Asp Ala Val Arg Leu Val Val Ala Arg Gly Gly Leu Met Gly
705 710 715 720

Gly Leu Pro Val Gly Gly Gly Met Trp Ser Val Gly Ala Ser Glu Ser
725 730 735

Val Val Arg Gly Val Val Glu Gly Leu Gly Glu Trp Val Ser Val Ala
740 745 750

Ala Val Asn Gly Pro Arg Ser Val Val Leu Ser Gly Asp Val Gly Val
755 760 765

Leu Glu Ser Val Val Ala Ser Leu Met Gly Asp Gly Val Glu Cys Arg
770 775 780

Arg Leu Asp Val Ser His Gly Phe His Ser Val Leu Met Glu Pro Val
785 790 795 800

Leu Gly Glu Phe Arg Gly Val Val Glu Ser Leu Glu Phe Gly Arg Val
805 810 815

Arg Pro Gly Val Val Val Val Ser Ser Val Ser Gly Gly Val Val Gly
820 825 830

Ser Gly Glu Leu Gly Asp Pro Gly Tyr Trp Val Arg His Ala Arg Glu
835 840 845

Ala Val Arg Phe Ala Asp Gly Val Gly Val Val Arg Gly Leu Gly Val
850 855 860

Gly Thr Leu Val Glu Val Gly Pro His Gly Val Leu Thr Gly Met Ala
865 870 875 880

Gly Glu Cys Leu Gly Ala Gly Asp Asp Val Val Val Val Pro Ala Met
885 890 895

Arg Arg Gly Arg Ala Glu Arg Glu Val Phe Glu Ala Ala Leu Ala Thr
900 905 910

Val Phe Thr Arg Asp Ala Gly Leu Asp Ala Thr Thr Leu His Thr Gly
915 920 925

Ser Thr Gly Arg Arg Ile Asp Leu Pro Thr Tyr Pro Phe Gln His Asp

930 935 940

Arg Tyr Trp Leu Ala Ala Pro Ser Arg Pro Arg Thr Asp Gly Leu Ser
945 950 955 960

Ala Ala Gly Leu Arg Glu Val Glu His Pro Leu Leu Thr Ala Ala Val
965 970 975

Glu Leu Pro Gly Thr Asp Thr Glu Val Trp Thr Gly Arg Ile Ser Ala
980 985 990

Ala Asp Leu Pro Trp Leu Ala Asp His Leu Val Trp Asp Arg Gly Val
995 1000 1005

Val Pro Gly Thr Ala Leu Leu Glu Thr Val Leu Gln Val Gly Ser Arg
1010 1015 1020

Ile Gly Leu Pro Arg Val Ala Glu Leu Val Leu Glu Thr Pro Leu Thr
1025 1030 1035 1040

Trp Thr Ser Asp Arg Pro Leu Gln Val Arg Ile Val Val Thr Ala Ala
1045 1050 1055

Ala Thr Ala Pro Gly Gly Ala Arg Glu Leu Thr Leu His Ser Arg Pro
1060 1065 1070

Glu Pro Val Ala Ala Ser Ser Ser Ser Pro Ser Pro Ala Ser Pro Arg
1075 1080 1085

His Leu Thr Ala Gln Glu Ser Asp Asp Asp Trp Thr Arg His Ala Ser
1090 1095 1100

Gly Leu Leu Ala Pro Ala Ala Gly Leu Ala Asp Asp Phe Ala Glu Leu
1105 1110 1115 1120

Thr Gly Ala Trp Pro Pro Val Gly Ala Glu Pro Leu Asp Leu Ala Gly
1125 1130 1135

Gln Tyr Pro Leu Phe Ala Ala Ala Gly Val Arg Tyr Glu Gly Ala Phe
1140 1145 1150

Arg Gly Leu Arg Ala Ala Trp Arg Arg Gly Asp Glu Val Phe Ala Asp
1155 1160 1165

Val Arg Leu Pro Asp Ala His Ala Val Asp Ala Asp Arg Tyr Gly Val
1170 1175 1180

His Pro Ala Leu Leu Asp Ala Val Leu His Pro Ile Ala Ser Leu Asp
1185 1190 1195 1200

Pro Leu Gly Asp Gly Gly His Gly Leu Leu Pro Phe Ser Trp Thr Asp
1205 1210 1215

Val Gln Gly His Gly Ala Gly Gly His Ala Leu Arg Val Arg Val Ala
1220 1225 1230

Ala Val Asp Gly Gly Ala Val Ser Val Thr Ala Ala Asp His Ala Gly
1235 1240 1245

Asn Pro Val Leu Ser Ala Arg Ser Leu Ala Leu Arg Arg Ile Thr Ala

1250 1255 1260

Asp Arg Leu Pro Ala Ala Pro Val Ala Pro Leu Tyr Arg Val Asp Trp
1265 1270 1275 1280

Leu Pro Phe Pro Gly Pro Val Pro Val Ser Ala Gly Gly Arg Trp Ala
1285 1290 1295

Val Val Gly Pro Glu Ala Glu Ala Thr Ala Ala Gly Leu Arg Ala Val
1300 1305 1310

Gly Leu Asp Val Arg Thr His Ala Leu Pro Leu Gly Glu Pro Leu Pro
1315 1320 1325

Pro Gln Ala Gly Thr Asp Ala Glu Val Ile Ile Leu Asp Leu Thr Thr
1330 1335 1340

Thr Ala Ala Gly Arg Thr Ala Ser Asp Gly Gly Arg Leu Ser Leu Leu
1345 1350 1355 1360

Asp Glu Val Arg Ala Thr Val Arg Arg Thr Leu Glu Ala Val Gln Ala
1365 1370 1375

Arg Leu Ala Asp Thr Glu Thr Ala Pro Asp Val Asp Val Arg Thr Ala
1380 1385 1390

Ala Arg Pro Arg Thr Ala Ala Arg Thr Ser Pro Arg Val Asp Thr Arg
1395 1400 1405

Thr Gly Ala Arg Thr Ala Asp Gly Pro Arg Leu Val Val Leu Thr Arg
1410 1415 1420

Gly Ala Ala Gly Pro Glu Gly Gly Ala Ala Asp Pro Ala Gly Ala Ala
1425 1430 1435 1440

Val Trp Gly Leu Val Arg Val Ala Gln Ala Glu Gln Pro Gly Arg Phe
1445 1450 1455

Thr Leu Val Asp Val Asp Gly Thr Gln Ala Ser Leu Arg Ala Leu Pro
1460 1465 1470

Gly Leu Leu Ala Thr Asp Ala Gly Gln Ser Ala Val Arg Asp Gly Arg
1475 1480 1485

Val Thr Val Pro Arg Leu Val Pro Val Ala Asp Pro Val Pro His Gly
1490 1495 1500

Gly Gly Thr Ala Ala Asp Gly Thr Gly Ala Gly Glu Pro Ser Ala Thr
1505 1510 1515 1520

Leu Asp Pro Glu Gly Thr Val Leu Ile Thr Gly Gly Thr Gly Ala Leu
1525 1530 1535

Ala Ala Glu Thr Ala Arg His Leu Val Asp Arg His Lys Val Arg His
1540 1545 1550

Leu Leu Leu Val Gly Arg Arg Gly Pro Asp Ala Pro Gly Val Asp Arg
1555 1560 1565

Leu Val Ala Glu Leu Thr Glu Ser Gly Ala Glu Val Ala Val Arg Ala

1570 1575 1580

Cys Asp Val Thr Asp Arg Asp Ala Leu Arg Arg Leu Leu Asp Ala Leu
1585 1590 1595 1600

Pro Asp Glu His Pro Leu Thr Cys Val Val His Thr Ala Gly Val Leu
1605 1610 1615

Asp Asp Gly Val Leu Ser Ala Gln Thr Ala Glu Arg Ile Asp Thr Val
1620 1625 1630

Leu Arg Pro Lys Ala Asp Ala Ala Val His Leu Asp Glu Leu Thr Arg
1635 1640 1645

Glu Ile Gly Arg Val Pro Leu Val Leu Tyr Ser Ser Val Ser Ala Thr
1650 1655 1660

Leu Gly Ser Ala Gly Gln Ala Gly Tyr Ala Ala Ala Asn Ala Phe Met
1665 1670 1675 1680

Asp Ala Leu Ala Ala Arg Arg Cys Ala Ala Gly His Pro Ala Leu Ser
1685 1690 1695

Leu Gly Trp Gly Trp Trp Ser Gly Val Gly Leu Ala Thr Gly Leu Asp
1700 1705 1710

Gly Ala Asp Ala Ala Arg Val Arg Arg Ser Gly Leu Ala Pro Leu Asp
1715 1720 1725

Ala Gly Ala Ala Leu Asp Leu Leu Asp Arg Ala Leu Thr Arg Pro Glu
1730 1735 1740

Pro Ala Leu Leu Pro Val Arg Leu Asp Leu Arg Ala Ala Ala Gly Ala
1745 1750 1755 1760

Thr Ala Leu Pro Glu Val Leu Arg Asp Leu Ala Gly Val Pro Ala Asp
1765 1770 1775

Ala Arg Ser Thr Pro Gly Ala Ala Ala Gly Thr Gly Asp Glu Asp Gly
1780 1785 1790

Ala Val Arg Pro Ala Pro Ala Pro Ala Asp Ala Ala Gly Thr Leu Ala
1795 1800 1805

Ala Arg Leu Ala Gly Arg Ser Ala Pro Glu Arg Thr Ala Leu Leu Leu
1810 1815 1820

Asp Leu Val Arg Thr Glu Val Ala Ala Val Leu Gly His Gly Asp Pro
1825 1830 1835 1840
Ala Ala Ile Gly Ala Ala Arg Thr Phe Lys Asp Ala Gly Phe Asp Ser
1845 1850 1855

Leu Thr Ala Val Asp Leu Arg Asn Arg Leu Asn Thr Arg Thr Gly Leu
1860 1865 1870

Arg Leu Pro Ala Thr Leu Val Phe Asp His Pro Thr Pro Leu Ala Leu
1875 1880 1885

Ala Glu Leu Leu Leu Asp Gly Leu Glu Ala Ala Gly Pro Ala Glu Pro

1890 1895 1900

Ala Ala Glu Val Pro Asp Glu Ala Ala Gly Ala Glu Thr Leu Ser Gly
1905 1910 1915 1920

Val Ile Asp Arg Leu Glu Arg Ser Leu Ala Ala Thr Asp Asp Gly Asp
1925 1930 1935

Ala Arg Val Arg Ala Ala Arg Arg Leu Arg Gly Leu Leu Asp Ala Leu
1940 1945 1950

Pro Ala Gly Pro Gly Ala Ala Ser Gly Pro Asp Ala Gly Glu His Ala
1955 1960 1965

Pro Gly Arg Gly Asp Val Val Ile Asp Arg Leu Arg Ser Ala Ser Asp
1970 1975 1980

Asp Asp Leu Phe Asp Leu Leu Asp Ser Asp Phe Gln
1985 1990 1995

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3724 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met Ser Ala Thr Asn Glu Glu Lys Leu Arg Glu Tyr Leu Arg Arg Ala
1 5 10 15

Met Ala Asp Leu His Ser Ala Arg Glu Arg Leu Arg Glu Val Glu Ser
20 25 30

Ala Ser Arg Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro
35 40 45

Gly Gly Val Ala Ser Pro Glu Glu Leu Trp Asp Leu Val Ala Ala Gly
50 55 60

Thr Asp Ala Ile Ser Pro Phe Pro Val Asp Arg Gly Trp Asp Ala Glu
65 70 75 80

Gly Leu Tyr Asp Pro Glu Pro Gly Val Pro Gly Lys Ser Tyr Val Arg
85 90 95

Glu Gly Gly Phe Leu His Ser Ala Ala Glu Phe Asp Ala Glu Phe Phe
100 105 110

Gly Ile Ser Pro Arg Glu Ala Ala Ala Met Asp Pro Gln Gln Arg Leu
115 120 125

Leu Leu Glu Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Val Pro
130 135 140

Ala Ser Leu Arg Gly Thr Arg Thr Gly Val Phe Thr Gly Val Met Tyr
145 150 155 160

His Asp Tyr Gly Ser His Gln Val Gly Thr Ala Ala Asp Pro Ser Gly
165 170 175

Gln Leu Gly Leu Gly Thr Ala Gly Ser Val Ala Ser Gly Arg Val Ala
180 185 190

Tyr Thr Leu Gly Leu Gln Gly Pro Ala Val Thr Met Asp Thr Ala Cys
195 200 205

Ser Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg
210 215 220

Gly Glu Cys Asp Leu Ala Leu Ala Gly Gly Ala Thr Val Leu Ala Thr
225 230 235 240

Pro Thr Val Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp
245 250 255

Gly Arg Cys Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala
260 265 270

Glu Gly Ala Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg
275 280 285

Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln
290 295 300

Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln
305 310 315 320

Arg Val Ile Arg Asp Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp
325 330 335

Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Pro Leu Gly Asp Pro
340 345 350

Ile Glu Ala Gly Ala Leu Met Ala Thr Tyr Gly Ser Glu Arg Val Gly
355 360 365

Asp Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Thr Gln
370 375 380

Ala Ala Ala Gly Ala Ala Gly Val Ile Lys Met Val Gln Ala Leu Arg
385 390 395 400

Gln Ser Glu Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ala Lys
405 410 415

Val Glu Trp Asp Ala Gly Ala Val Gln Leu Leu Thr Gly Val Arg Pro
420 425 430

Trp Pro Arg Arg Glu His Arg Pro Arg Arg Ala Ala Val Ser Ala Phe
435 440 445

Gly Val Ser Gly Thr Asn Ala His Val Ile Ile Glu Glu Pro Pro Ala
450 455 460

Ala Gly Asp Thr Ser Pro Ala Gly Asp Thr Pro Glu Pro Gly Glu Ala
465 470 475 480

Thr Ala Ser Pro Ser Thr Ala Ala Gly Pro Ser Ser Pro Ser Ala Val
485 490 495

Ala Gly Pro Leu Ser Pro Ser Ser Pro Ala Val Val Trp Pro Leu Ser
500 505 510

Ala Glu Thr Ala Pro Ala Leu Arg Ala Gln Ala Ala Arg Leu Arg Ala
515 520 525

His Leu Glu Arg Leu Pro Gly Thr Ser Pro Thr Asp Ile Gly His Ala
530 535 540

Leu Ala Ala Glu Arg Ala Ala Leu Thr Arg Arg Val Val Leu Leu Gly
545 550 555 560

Asp Asp Gly Ala Pro Val Asp Ala Leu Ala Ala Leu Ala Ala Gly Glu
565 570 575

Thr Thr Pro Asp Ala Val His Gly Thr Ala Ala Asp Ile Arg Arg Val
580 585 590

Ala Phe Val Phe Pro Gly Gln Gly Ser Gln Trp Ala Gly Met Gly Ala
595 600 605

Glu Leu Leu Asp Thr Ala Pro Ala Phe Ala Ala Glu Leu Asp Arg Cys
610 615 620

Gln Gly Ala Leu Ser Pro Tyr Val Asp Trp Asn Leu Ala Asp Val Leu
625 630 635 640

Arg Gly Ala Pro Ala Ala Pro Gly Leu Asp Arg Val Asp Val Val Gln
645 650 655

Pro Ala Thr Phe Ala Val Met Val Gly Leu Ala Ala Leu Trp Arg Ser
660 665 670

Leu Gly Val Glu Pro Ala Ala Val Ile Gly His Ser Gln Gly Glu Ile
675 680 685

Ala Ala Ala Cys Val Ala Gly Ala Leu Ser Leu Glu Asp Ala Ala Arg
690 695 700

Ile Val Ala Leu Arg Ser Gln Val Ile Ala Arg Glu Leu Ala Gly Arg
705 710 715 720

Gly Gly Met Ala Ser Val Ala Leu Pro Ala Ala Glu Val Glu Ala Arg
725 730 735

Leu Ala Gly Gly Val Glu Ile Ala Ala Val Asn Gly Pro Gly Ser Thr
740 745 750

Val Val Cys Gly Glu Pro Gly Ala Leu Glu Ala Leu Leu Val Thr Leu
755 760 765

Glu Ser Glu Gly Thr Arg Val Arg Arg Ile Asp Val Asp Tyr Ala Ser
770 775 780

His Ser His Tyr Val Glu Ser Ile Arg Ala Glu Leu Ala Thr Val Leu
785 790 795 800

Gly Pro Val Arg Pro Arg Arg Gly Asp Val Pro Phe Tyr Ser Thr Val
805 810 815

Glu Ala Ala Leu Leu Asp Thr Ala Thr Leu Asp Ala Asp Tyr Trp Tyr
820 825 830

Arg Asn Leu Arg Leu Pro Val Arg Phe Glu Pro Thr Val Arg Ala Met
835 840 845

Leu Asp Asp Gly Val Asp Ala Phe Val Glu Cys Ser Ala His Pro Val
850 855 860

Leu Thr Val Gly Val Arg Gln Thr Val Glu Ser Ala Gly Gly Ala Val
865 870 875 880

Pro Ala Leu Ala Ser Leu Arg Arg Asp Glu Gly Gly Leu Arg Arg Phe
885 890 895

Leu Thr Ser Ala Ala Glu Ala Gln Val Val Gly Val Pro Val Asp Trp
900 905 910

Ala Thr Leu Arg Pro Gly Ala Gly Arg Val Asp Leu Pro Thr Tyr Ala
915 920 925

Phe Gln Arg Glu Arg His Trp Val Gly Pro Ala Arg Pro Asp Ser Ala
930 935 940

Ala Thr Ala Ala Thr Thr Gly Asp Asp Ala Pro Glu Pro Gly Asp Arg
945 950 955 960

Leu Gly Tyr His Val Ala Trp Lys Gly Leu Arg Ser Thr Thr Gly Gly
965 970 975

Trp Arg Pro Gly Leu Arg Leu Leu Ile Val Pro Thr Gly Asp Gln Tyr
980 985 990

Thr Ala Leu Ala Asp Thr Leu Glu Gln Ala Val Ala Ser Phe Gly Gly
995 1000 1005

Thr Val Arg Arg Val Ala Phe Asp Pro Ala Arg Thr Gly Arg Ala Glu
1010 1015 1020

Leu Phe Gly Leu Leu Glu Thr Glu Ile Asn Gly Asp Thr Ala Val Thr
1025 1030 1035 1040

Gly Val Val Ser Leu Leu Gly Leu Cys Thr Asp Gly Arg Pro Asp His
1045 1050 1055

Pro Ala Val Pro Val Ala Val Thr Ala Thr Leu Ala Leu Val Gln Ala
1060 1065 1070

Leu Ala Asp Leu Gly Ser Thr Ala Pro Leu Trp Thr Val Thr Cys Gly
1075 1080 1085

Ala Val Ala Thr Ala Pro Asp Glu Leu Pro Cys Thr Ala Gly Ala Gln
1090 1095 1100

Leu Trp Gly Leu Gly Arg Val Ala Ala Leu Glu Leu Pro Glu Val Trp
1105 1110 1115 1120

Gly Gly Leu Ile Asp Leu Pro Ala Arg Pro Asp Ala Arg Val Leu Asp
1125 1130 1135

Arg Leu Ala Gly Val Leu Ala Glu Pro Gly Gly Glu Asp Gln Ile Ala
1140 1145 1150

Val Arg Met Ala Gly Val Phe Gly Arg Arg Val Leu Arg Asn Pro Ala
1155 1160 1165

Asp Ser Arg Pro Pro Ala Trp Arg Ala Arg Gly Thr Val Leu Ile Ala
1170 1175 1180

Gly Asp Leu Thr Thr Val Pro Gly Arg Leu Val Arg Ser Leu Leu Glu
1185 1190 1195 1200

Asp Gly Ala Asp Arg Val Val Leu Ala Gly Pro Asp Ala Pro Ala Gln
1205 1210 1215

Ala Ala Ala Ala Gly Leu Thr Gly Val Ser Leu Val Pro Val Arg Cys
1220 1225 1230

Asp Val Thr Asp Arg Ala Ala Leu Ala Ala Leu Leu Asp Glu His Ala
1235 1240 1245

Pro Thr Val Ala Val His Ala Pro Pro Leu Val Pro Leu Ala Pro Leu
1250 1255 1260

Arg Glu Thr Ala Pro Gly Asp Ile Ala Ala Ala Leu Ala Ala Lys Thr
1265 1270 1275 1280

Thr Ala Ala Gly His Leu Val Asp Leu Ala Pro Ala Ala Gly Leu Asp
1285 1290 1295

Ala Leu Val Leu Phe Ser Ser Val Ser Gly Val Trp Gly Gly Ala Ala
1300 1305 1310

Gln Gly Gly Tyr Ala Ala Ala Ser Ala His Leu Asp Ala Leu Ala Glu
1315 1320 1325

Arg Ala Arg Ala Ala Gly Val Pro Ala Phe Ser Val Ala Trp Ser Pro
1330 1335 1340

Trp Ala Gly Gly Thr Pro Ala Asp Gly Ala Glu Ala Glu Phe Leu Ser
1345 1350 1355 1360

Arg Arg Gly Leu Ala Pro Leu Asp Pro Asp Gln Ala Val Arg Thr Leu
1365 1370 1375

Arg Arg Met Leu Glu Arg Gly Ser Ala Cys Gly Ala Val Ala Asp Val
1380 1385 1390

Glu Trp Ser Arg Phe Ala Ala Ser Tyr Thr Trp Val Arg Pro Ala Val
1395 1400 1405

Leu Phe Asp Asp Ile Pro Asp Val Gln Arg Leu Arg Ala Ala Glu Leu
1410 1415 1420

Ala Pro Ser Thr Gly Asp Ser Thr Thr Ser Glu Leu Val Arg Glu Leu
1425 1430 1435 1440

Thr Ala Gln Ser Gly His Lys Arg His Ala Thr Leu Leu Arg Leu Val
1445 1450 1455

Arg Ala His Ala Ala Ala Val Leu Gly Gln Ser Ser Gly Asp Ala Val
1460 1465 1470

Ser Ser Ala Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala
1475 1480 1485

Leu Glu Leu Arg Asp Arg Leu Ser Thr Ser Thr Gly Leu Lys Leu Pro
1490 1495 1500

Thr Ser Leu Val Phe Asp His Ser Ser Pro Ala Ala Leu Ala Arg His
1505 1510 1515 1520
Leu Gly Glu Glu Leu Leu Gly Arg Asn Asp Thr Ala Asp Arg Ala Gly
1525 1530 1535

Pro Asp Thr Pro Val Arg Thr Asp Glu Pro Ile Ala Ile Ile Gly Met
1540 1545 1550

Ala Cys Arg Leu Pro Gly Gly Val Gln Ser Pro Glu Asp Leu Trp Asp
1555 1560 1565

Leu Leu Thr Gly Gly Thr Asp Ala Ile Thr Pro Phe Pro Thr Asn Arg
1570 1575 1580

Gly Trp Asp Asn Glu Thr Leu Tyr Asp Pro Asp Pro Asp Ser Pro Gly
1585 1590 1595 1600

His His Thr Tyr Val Arg Glu Gly Gly Phe Leu His Asp Ala Ala Glu
1605 1610 1615

Phe Asp Pro Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met
1620 1625 1630

Asp Pro Gln Gln Arg Leu Ile Leu Glu Thr Ser Trp Glu Ser Phe Glu
1635 1640 1645

Arg Ala Gly Ile Asp Pro Val Glu Leu Arg Gly Ser Arg Thr Gly Val
1650 1655 1660

Phe Val Gly Thr Asn Gly Gln His Tyr Val Pro Leu Leu Gln Asp Gly
1665 1670 1675 1680

Asp Glu Asn Phe Asp Gly Tyr Ile Ala Thr Gly Asn Ser Ala Ser Val
1685 1690 1695

Met Ser Gly Arg Leu Ser Tyr Val Phe Gly Leu Glu Gly Pro Ala Val
1700 1705 1710

Thr Val Asp Thr Ala Cys Ser Ala Ser Leu Ala Ala Leu His Leu Ala
1715 1720 1725

Val Gln Ser Leu Arg Arg Gly Glu Cys Asp Tyr Ala Leu Ala Gly Gly
1730 1735 1740

Ala Thr Val Met Ser Thr Pro Glu Met Leu Val Glu Phe Ala Arg Gln
1745 1750 1755 1760

Arg Ala Val Ser Pro Asp Gly Arg Ser Lys Ala Phe Ala Glu Ala Ala
1765 1770 1775

Asp Gly Val Gly Leu Ala Glu Gly Ala Gly Met Leu Leu Val Glu Arg
1780 1785 1790

Leu Ser Glu Ala Gln Lys Lys Gly His Pro Val Leu Ala Val Val Arg
1795 1800 1805

Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro
1810 1815 1820

Ser Gly Pro Ala Gln Gln Arg Val Ile Arg Glu Ala Leu Ala Asp Ala
1825 1830 1835 1840

Gly Leu Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly
1845 1850 1855

Thr Pro Leu Gly Asp Pro Ile Glu Ala Gly Ala Leu Leu Ala Thr Tyr
1860 1865 1870

Gly Arg Asp Arg Arg Asp Gly Pro Leu Trp Leu Gly Ser Leu Lys Ser
1875 1880 1885

Asn Ile Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys
1890 1895 1900

Met Val Leu Ala Leu Arg His Gly Glu Leu Pro Arg Thr Leu His Ala
1905 1910 1915 1920

Ser Thr Ala Ser Ser Arg Ile Asp Trp Asp Ala Gly Ala Val Glu Leu
1925 1930 1935

Leu Asp Glu Ala Arg Pro Trp Leu Gln Arg Ala Glu Gly Pro Arg Arg
1940 1945 1950

Ala Gly Ile Ser Ser Phe Gly Ile Ser Gly Thr Asn Ala His Leu Val
1955 1960 1965

Ile Glu Glu Pro Pro Glu Pro Thr Ala Pro Glu Leu Leu Ala Pro Glu
1970 1975 1980

Pro Ala Ala Asp Gly Asp Val Trp Ser Glu Glu Trp Trp His Glu Val
1985 1990 1995 2000

Thr Val Pro Leu Met Met Ser Ala His Asn Glu Ala Ala Leu Arg Asp
2005 2010 2015

Gln Ala Arg Arg Leu Arg Ala Asp Leu Leu Ala His Pro Glu Leu His
2020 2025 2030

Pro Ala Asp Val Gly Tyr Thr Leu Ile Thr Thr Arg Thr Arg Phe Glu
2035 2040 2045

Gln Arg Ala Ala Val Val Gly Glu Asn Phe Thr Glu Leu Ile Ala Ala
2050 2055 2060

Leu Asp Asp Leu Val Glu Gly Arg Pro His Pro Leu Val Leu Arg Gly
2065 2070 2075 2080

Thr Ala Gly Thr Ser Asp Gln Val Val Phe Val Phe Pro Gly Gln Gly
2085 2090 2095

Ser Gln Trp Pro Glu Met Ala Asp Gly Leu Leu Ala Arg Ser Ser Gly
2100 2105 2110

Ser Gly Ser Phe Leu Glu Thr Ala Arg Ala Cys Asp Leu Ala Leu Arg
2115 2120 2125

Pro His Leu Gly Trp Ser Val Leu Asp Val Leu Arg Arg Glu Pro Gly
2130 2135 2140

Ala Pro Ser Leu Asp Arg Val Asp Val Val Gln Pro Val Leu Phe Thr
2145 2150 2155 2160

Met Met Val Ser Leu Ala Glu Thr Trp Arg Ser Leu Gly Val Glu Pro
2165 2170 2175

Ala Ala Val Val Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val
2180 2185 2190

Ala Gly Ala Leu Thr Leu Asp Asp Ala Ala Arg Ile Val Ala Leu Arg
2195 2200 2205

Ser Gln Ala Trp Leu Arg Leu Ala Gly Lys Gly Gly Met Val Ala Val
2210 2215 2220

Thr Leu Ser Glu Arg Asp Leu Arg Pro Arg Leu Glu Pro Trp Ser Asp
2225 2230 2235 2240

Arg Leu Ala Val Ala Ala Val Asn Gly Pro Glu Thr Cys Ala Val Ser
2245 2250 2255

Gly Asp Pro Asp Ala Leu Ala Glu Leu Val Ala Glu Leu Gly Ala Glu
2260 2265 2270

Gly Val His Ala Arg Pro Ile Pro Gly Val Asp Thr Ala Gly His Ser
2275 2280 2285

Pro Gln Val Asp Thr Leu Glu Ala His Leu Arg Lys Val Leu Ala Pro
2290 2295 2300

Val Ala Pro Arg Thr Ser Asp Ile Pro Phe Tyr Ser Thr Val Thr Gly
2305 2310 2315 2320

Gly Leu Ile Asp Thr Ala Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn
2325 2330 2335

Met Arg Glu Pro Val Glu Phe Glu Gln Ala Thr Arg Ala Leu Ile Ala
2340 2345 2350

Asp Gly His Asp Val Phe Leu Glu Ser Ser Pro His Pro Met Leu Ala
2355 2360 2365

Val Ser Leu Gln Glu Thr Ile Ser Asp Ala Gly Ser Pro Ala Ala Val
2370 2375 2380

Leu Gly Thr Leu Arg Arg Gly Gln Gly Gly Pro Arg Trp Leu Gly Val
2385 2390 2395 2400

Ala Leu Cys Arg Ala Tyr Thr His Gly Leu Glu Ile Asp Ala Glu Ala
2405 2410 2415

Ile Phe Gly Pro Asp Ser Arg Gln Val Glu Leu Pro Thr Tyr Pro Phe
2420 2425 2430

Gln Arg Glu Arg Tyr Trp Tyr Ser Pro Gly His Arg Gly Asp Asp Pro
2435 2440 2445

Ala Ser Leu Gly Leu Asp Ala Val Asp His Pro Leu Leu Gly Ser Gly
2450 2455 2460

Val Glu Leu Pro Glu Ser Gly Asp Arg Met Tyr Thr Ala Arg Leu Gly
2465 2470 2475 2480

Ala Asp Thr Thr Pro Trp Leu Ala Asp His Ala Leu Leu Gly Ser Pro
2485 2490 2495

Leu Leu Pro Gly Ala Ala Phe Ala Asp Leu Ala Leu Trp Ala Gly Arg
2500 2505 2510

Gln Ala Gly Thr Gly Arg Val Glu Glu Leu Thr Leu Ala Ala Pro Leu
2515 2520 2525

Val Leu Pro Gly Ser Gly Gly Val Arg Leu Arg Leu Asn Val Gly Ala
2530 2535 2540

Pro Gly Thr Asp Asp Ala Arg Arg Phe Ala Val His Ala Arg Ala Glu
2545 2550 2555 2560

Gly Ala Thr Asp Trp Thr Leu His Ala Glu Gly Leu Leu Thr Ala Gln
2565 2570 2575

Asp Thr Ala Asp Ala Pro Asp Ala Ser Ala Ala Thr Pro Pro Pro Gly
2580 2585 2590

Ala Glu Gln Leu Asp Ile Gly Asp Phe Tyr Gln Arg Phe Ser Glu Leu
2595 2600 2605

Gly Tyr Gly Tyr Gly Pro Phe Phe Arg Gly Leu Val Ser Ala His Arg
2610 2615 2620

Cys Gly Pro Asp Ile His Ala Glu Val Ala Leu Pro Val Gln Ala Gln
2625 2630 2635 2640

Gly Asp Ala Ala Arg Phe Gly Ile His Pro Ala Leu Leu Asp Ala Ala
2645 2650 2655

Leu Gln Thr Met Ser Leu Gly Gly Phe Phe Pro Glu Asp Gly Arg Val
2660 2665 2670

Arg Met Pro Phe Ala Leu Arg Gly Val Arg Leu Tyr Arg Ala Gly Ala
2675 2680 2685

Asp Arg Leu His Val Arg Val Ser Pro Val Ser Glu Asp Ala Val Arg
2690 2695 2700

Ile Arg Cys Ala Asp Gly Glu Gly Arg Pro Val Ala Glu Ile Glu Ser
2705 2710 2715 2720

Phe Ile Met Arg Pro Val Asp Pro Gly Gln Leu Leu Gly Gly Arg Pro
2725 2730 2735

Val Gly Ala Asp Ala Leu Phe Arg Ile Ala Trp Arg Glu Leu Ala Ala
2740 2745 2750

Gly Pro Gly Thr Arg Thr Gly Asp Gly Thr Pro Pro Pro Val Arg Trp
2755 2760 2765

Val Leu Ala Gly Pro Asp Ala Leu Gly Leu Ala Glu Ala Ala Asp Ala
2770 2775 2780

His Leu Pro Ala Val Pro Gly Pro Asp Gly Ala Leu Pro Ser Pro Thr
2785 2790 2795 2800

Gly Arg Pro Ala Pro Asp Ala Val Val Phe Ala Val Arg Ala Gly Thr
2805 2810 2815

Gly Asp Val Ala Ala Asp Ala His Thr Val Ala Cys Arg Val Leu Asp
2820 2825 2830

Leu Val Gln Arg Arg Leu Ala Ala Pro Glu Gly Pro Asp Gly Ala Arg
2835 2840 2845

Leu Val Val Ala Thr Arg Gly Ala Val Ala Val Arg Asp Asp Ala Glu
2850 2855 2860

Val Asp Asp Pro Ala Ala Ala Ala Ala Trp Gly Leu Leu Arg Ser Ala
2865 2870 2875 2880

Gln Ala Glu Glu Pro Gly Arg Phe Leu Leu Val Asp Leu Asp Asp Asp
2885 2890 2895

Pro Ala Ser Ala Arg Ala Leu Thr Asp Ala Leu Ala Ser Gly Glu Pro
2900 2905 2910

Gln Thr Ala Val Arg Ala Gly Thr Val Tyr Val Pro Arg Leu Glu Arg
2915 2920 2925

Ala Ala Asp Arg Thr Asp Gly Pro Leu Thr Pro Pro Asp Asp Gly Ala
2930 2935 2940

Trp Arg Leu Gly Arg Gly Thr Asp Leu Thr Leu Asp Gly Leu Ala Leu
2945 2950 2955 2960

Val Pro Ala Pro Asp Ala Glu Ala Pro Leu Glu Pro Gly Gln Val Arg
2965 2970 2975

Val Ala Val Arg Ala Ala Gly Val Asn Phe Arg Asp Ala Leu Ile Ala
2980 2985 2990

Leu Gly Met Tyr Pro Gly Glu Ala Glu Met Gly Thr Glu Gly Ala Gly
2995 3000 3005

Thr Val Val Glu Val Gly Pro Gly Val Thr Gly Val Ala Val Gly Asp
3010 3015 3020

Arg Val Leu Gly Leu Trp Asp Gly Gly Leu Gly Pro Leu Cys Val Ala
3025 3030 3035 3040

Asp His Arg Leu Leu Ala Pro Val Pro Asp Gly Trp Ser Tyr Ala Gln
3045 3050 3055

Ala Ala Ser Val Pro Ala Val Phe Leu Ser Ala Tyr Tyr Gly Leu Val
3060 3065 3070

Thr Leu Ala Gly Leu Arg Pro Gly Glu Arg Val Leu Val His Ala Ala
3075 3080 3085

Ala Gly Gly Val Gly Met Ala Ala Val Gln Ile Ala Arg His Leu Gly
3090 3095 3100

Ala Glu Val Leu Ala Thr Ala Ser Pro Gly Lys Trp Asp Ala Leu Arg
3105 3110 3115 3120

Ala Met Gly Ile Thr Asp Asp His Leu Ala Ser Ser Arg Thr Leu Asp
3125 3130 3135

Phe Ala Thr Ala Phe Thr Gly Ala Asp Gly Thr Ser Arg Ala Asp Val
3140 3145 3150

Val Leu Asn Ser Leu Thr Lys Glu Phe Val Asp Ala Ser Leu Gly Leu
3155 3160 3165

Leu Arg Pro Gly Gly Arg Phe Leu Glu Leu Gly Lys Thr Asp Val Arg
3170 3175 3180

Asp Pro Glu Arg Ile Ala Ala Glu His Pro Gly Val Arg Tyr Arg Ala
3185 3190 3195 3200

Phe Asp Leu Asn Glu Ala Gly Pro Asp Ala Leu Gly Arg Leu Leu Arg
3205 3210 3215

Glu Leu Met Asp Leu Phe Ala Ala Gly Val Leu His Pro Leu Pro Val
3220 3225 3230

Val Thr His Asp Val Arg Arg Ala Ala Asp Ala Leu Arg Thr Ile Ser
3235 3240 3245

Gln Ala Arg His Thr Gly Lys Leu Val Leu Thr Met Pro Pro Ala Trp
3250 3255 3260

His Pro Tyr Gly Thr Val Leu Val Thr Gly Gly Thr Gly Ala Leu Gly
3265 3270 3275 3280
Ser Arg Ile Ala Arg His Leu Ala Ser Arg His Gly Val Arg Arg Leu
3285 3290 3295

Leu Ile Ala Ala Arg Arg Gly Pro Asp Gly Glu Gly Ala Ala Glu Leu
3300 3305 3310

Val Ala Asp Leu Ala Ala Leu Gly Ala Ser Ala Thr Val Val Ala Cys
3315 3320 3325

Asp Val Ser Asp Ala Asp Ala Val Arg Gly Leu Leu Ala Gly Ile Pro
3330 3335 3340

Ala Asp His Pro Leu Thr Ala Val Val His Ser Thr Gly Val Leu Asp
3345 3350 3355 3360

Asp Gly Val Leu Pro Gly Leu Thr Pro Glu Arg Met Arg Arg Val Leu
3365 3370 3375

Arg Pro Lys Val Glu Ala Ala Val His Leu Asp Glu Leu Thr Arg Asp
3380 3385 3390

Leu Asp Leu Ser Ala Phe Val Leu Phe Ser Ser Ser Ala Gly Leu Leu
3395 3400 3405

Gly Ser Pro Ala Gln Gly Asn Tyr Ala Ala Ala Asn Ala Thr Leu Asp
3410 3415 3420

Ala Leu Ala Ala Arg Arg Arg Ser Leu Gly Leu Pro Ser Val Ser Leu
3425 3430 3435 3440

Ala Trp Gly Leu Trp Ser Asp Thr Ser Arg Met Ala His Ala Leu Asp
3445 3450 3455

Gln Glu Ser Leu Gln Arg Arg Phe Ala Arg Ser Gly Phe Pro Pro Leu
3460 3465 3470

Ser Ala Thr Leu Gly Ala Ala Leu Phe Asp Ala Ala Leu Arg Val Asp
3475 3480 3485

Glu Ala Val Gln Val Pro Met Arg Phe Asp Pro Ala Ala Leu Arg Ala
3490 3495 3500

Thr Gly Ser Val Pro Ala Leu Leu Ser Asp Leu Val Gly Ser Ala Pro
3505 3510 3515 3520

Ala Thr Gly Ser Ala Ala Pro Ala Ser Gly Pro Leu Pro Ala Pro Asp
3525 3530 3535

Ala Gly Thr Val Gly Glu Pro Leu Ala Glu Arg Leu Ala Gly Leu Ser
3540 3545 3550

Ala Glu Glu Arg His Asp Arg Leu Leu Gly Leu Val Gly Glu His Val
3555 3560 3565

Ala Ala Val Leu Gly His Gly Ser Ala Ala Glu Val Arg Pro Asp Arg
3570 3575 3580

Pro Phe Arg Glu Val Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg
3585 3590 3595 3600

Asn Arg Met Ala Ala Val Thr Gly Val Arg Leu Pro Ala Thr Leu Val
3605 3610 3615

Phe Asp His Pro Thr Pro Ala Ala Leu Ser Ser His Leu Asp Gly Leu
3620 3625 3630

Leu Ala Pro Ala Gln Pro Val Thr Thr Thr Pro Leu Leu Ser Glu Leu
3635 3640 3645

Asp Arg Ile Glu Glu Ala Leu Ala Ala Leu Thr Pro Glu His Leu Ala
3650 3655 3660

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Glu Leu Ala Pro Ala Pro Asp Asp Arg Ala Glu Val Ala Leu Arg Leu
3665                3670                3675                3680

Asp Ala Leu Ala Asp Arg Trp Arg Ala Leu His Asp Gly Ala Pro Gly
                3685                3690                3695

Ala Asp Asp Asp Ile Thr Asp Val Leu Ser Ser Ala Asp Asp Asp Glu
            3700                3705                3710

Ile Phe Ala Phe Ile Asp Glu Arg Tyr Gly Thr Ser
        3715                3720
```

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1580 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

```
Met Ala Asn Glu Glu Lys Leu Arg Ala Tyr Leu Lys Arg Val Thr Gly
1               5                   10                  15

Glu Leu His Arg Ala Thr Glu Gln Leu Arg Ala Leu Asp Arg Arg Ala
            20                  25                  30

His Glu Pro Ile Ala Ile Val Gly Ala Ala Cys Arg Leu Pro Gly Gly
        35                  40                  45

Val Glu Ser Pro Asp Asp Leu Trp Glu Leu Leu His Ala Gly Ala Asp
    50                  55                  60

Ala Val Gly Pro Ala Pro Ala Asp Arg Gly Trp Asp Val Glu Gly Arg
65                  70                  75                  80

Tyr Ser Pro Asp Pro Asp Thr Pro Gly Thr Ser Tyr Cys Arg Glu Gly
                85                  90                  95

Gly Phe Val Gln Gly Ala Asp Arg Phe Asp Pro Ala Leu Phe Gly Ile
            100                 105                 110

Ser Pro Asn Glu Ala Leu Thr Met Asp Pro Gln Gln Arg Leu Leu Leu
        115                 120                 125

Glu Thr Ser Trp Glu Ala Leu Glu Arg Ala Gly Leu Asp Pro Gln Ser
    130                 135                 140

Leu Ala Gly Ser Arg Thr Gly Val Phe Ala Gly Ala Trp Glu Ser Gly
145                 150                 155                 160

Tyr Gln Lys Gly Val Glu Gly Leu Glu Ala Asp Leu Glu Ala Gln Leu
                165                 170                 175
Leu Ala Gly Ile Val Ser Phe Thr Ala Gly Arg Val Ala Tyr Ala Leu
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180 185 190

Gly Leu Glu Gly Pro Ala Leu Thr Ile Asp Thr Ala Cys Ser Ser Ser
195 200 205

Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly Glu Cys
210 215 220

Asp Leu Ala Leu Ala Gly Gly Ala Thr Val Ile Ala Asp Phe Ala Leu
225 230 235 240

Phe Thr Gln Phe Ser Arg Gln Arg Gly Leu Ala Pro Asp Gly Arg Cys
245 250 255

Lys Ala Phe Gly Glu Thr Ala Asp Gly Phe Gly Pro Ala Glu Gly Ala
260 265 270

Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His
275 280 285

Pro Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala
290 295 300

Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg Val Ile
305 310 315 320

Arg Glu Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp Val Asp Ala
325 330 335

Val Glu Ala His Gly Thr Gly Thr Pro Leu Gly Asp Pro Ile Glu Ala
340 345 350

Gly Ala Leu Met Ala Thr Tyr Gly His Glu Arg Thr Gly Asp Pro Leu
355 360 365

Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Thr Gln Ala Ala Ala
370 375 380

Gly Val Ala Gly Val Ile Lys Met Val Leu Ala Leu Arg His Gly Glu
385 390 395 400

Leu Pro Arg Thr Leu His Ala Ser Thr Ala Ser Ser Arg Ile Glu Trp
405 410 415

Asp Ala Gly Ala Val Glu Leu Leu Asp Glu Ala Arg Pro Trp Pro Arg
420 425 430

Arg Ala Glu Gly Pro Arg Arg Ala Gly Ile Ser Ser Phe Gly Ile Ser
435 440 445

Gly Thr Asn Ala His Leu Val Ile Glu Glu Glu Pro Pro Ala Arg Pro
450 455 460

Glu Pro Glu Glu Ala Ala Gln Pro Pro Ala Pro Ala Thr Thr Val Leu
465 470 475 480

Pro Leu Ser Ala Ala Gly Ala Arg Ser Leu Arg Glu Gln Ala Arg Arg
485 490 495

Leu Ala Ala His Leu Ala Gly His Glu Glu Ile Thr Ala Ala Asp Ala
500 505 510

Ala Arg Ser Ala Ala Thr Thr Arg Ala Ala Leu Ser His Arg Ala Ser
515 520 525

Val Leu Ala Asp Asp Arg Arg Ala Leu Ile Asp Arg Leu Thr Ala Leu
530 535 540

Ala Glu Asp Arg Lys Asp Pro Gly Val Thr Val Gly Glu Ala Gly Ser
545 550 555 560

Gly Arg Pro Pro Val Phe Val Phe Pro Gly Gln Gly Ser Gln Trp Thr
565 570 575

Gly Met Gly Ala Glu Leu Leu Asp Arg Ala Pro Val Phe Arg Ala Lys
580 585 590

Ala Glu Glu Cys Ala Arg Ala Leu Ala Ala His Leu Asp Trp Ser Val
595 600 605

Leu Asp Val Leu Arg Asp Ala Pro Gly Ala Pro Pro Ile Asp Arg Ala
610 615 620

Asp Val Val Gln Pro Thr Leu Phe Thr Met Met Val Ser Leu Ala Ala
625 630 635 640

Leu Trp Glu Ser His Gly Val Arg Pro Ala Ala Val Val Gly His Ser
645 650 655

Gln Gly Glu Ile Ala Ala Ala His Ala Ala Gly Ala Leu Ser Leu Asp
660 665 670

Asp Ala Ala Arg Val Ile Ala Glu Arg Ser Arg Leu Trp Lys Arg Leu
675 680 685

Ala Gly Asn Gly Gly Met Leu Ser Val Met Ala Pro Ala Asp Arg Val
690 695 700

Arg Glu Leu Met Glu Pro Trp Ala Glu Arg Met Ser Val Ala Ala Val
705 710 715 720

Asn Gly Pro Ala Ser Val Thr Val Ala Gly Asp Ala Arg Ala Leu Glu
725 730 735

Glu Phe Gly Gly Arg Leu Ser Ala Ala Gly Val Leu Arg Trp Pro Leu
740 745 750

Ala Gly Val Asp Phe Ala Gly His Ser Pro Gln Val Glu Gln Phe Arg
755 760 765

Ala Glu Leu Leu Asp Thr Leu Gly Thr Val Arg Pro Thr Ala Ala Arg
770 775 780

Leu Pro Phe Phe Ser Thr Val Thr Ala Ala Ala His Glu Pro Glu Gly
785 790 795 800

Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Met Arg Glu Pro Val Glu Phe
805 810 815

Ala Ser Thr Leu Arg Thr Leu Leu Arg Glu Gly His Arg Thr Phe Val
820 825 830

Glu Met Gly Pro His Pro Leu Leu Gly Ala Ala Ile Asp Glu Val Ala
835 840 845

Glu Ala Glu Gly Val His Ala Thr Ala Leu Ala Thr Leu His Arg Gly
850 855 860

Ser Gly Gly Leu Asp Arg Phe Arg Ser Ser Val Gly Ala Ala Phe Ala
865 870 875 880

His Gly Val Arg Val Asp Trp Asp Ala Leu Phe Glu Gly Ser Gly Ala
885 890 895

Arg Arg Val Pro Leu Pro Thr Tyr Ala Phe Ser Arg Asp Arg Tyr Trp
900 905 910

Leu Pro Thr Ala Ile Gly Arg Arg Ala Val Glu Ala Ala Pro Val Asp
915 920 925

Ala Ser Ala Pro Gly Arg Tyr Arg Val Thr Trp Thr Pro Val Ala Ser
930 935 940

Asp Asp Ser Gly Arg Pro Ser Gly Arg Trp Leu Leu Val Gln Thr Pro
945 950 955 960

Gly Thr Ala Pro Asp Glu Ala Asp Thr Ala Ala Ser Ala Leu Gly Ala
965 970 975

Ala Gly Val Val Val Glu Arg Cys Leu Leu Asp Pro Thr Glu Ala Ala
980 985 990

Arg Val Thr Leu Thr Glu Arg Leu Ala Glu Leu Asp Ala Gln Pro Glu
995 1000 1005

Gly Leu Ala Gly Val Leu Val Leu Pro Gly Arg Pro Gln Ser Thr Ala
1010 1015 1020

Pro Ala Asp Ala Ser Pro Leu Asp Pro Gly Thr Ala Ala Val Leu Leu
1025 1030 1035 1040

Val Val Gln Ala Val Pro Asp Ala Ala Pro Lys Ala Arg Ile Trp Val
1045 1050 1055

Val Thr Arg Gly Ala Val Ala Val Gly Ser Gly Glu Val Pro Cys Ala
1060 1065 1070

Val Gly Ala Arg Val Trp Gly Leu Gly Arg Val Ala Ala Leu Glu Val
1075 1080 1085

Pro Val Gln Trp Gly Gly Leu Val Asp Val Ala Val Gly Ala Gly Val
1090 1095 1100

Arg Glu Trp Arg Arg Val Val Gly Val Val Ala Gly Gly Gly Glu Asp
1105 1110 1115 1120

Gln Val Ala Val Arg Gly Gly Gly Val Phe Gly Arg Arg Leu Val Gly
1125 1130 1135

Val Gly Val Arg Gly Gly Ser Gly Val Trp Arg Ala Arg Gly Cys Val
1140 1145 1150

Val Val Thr Gly Gly Leu Gly Gly Val Gly Gly His Val Ala Arg Trp
1155 1160 1165

Leu Ala Arg Ser Gly Ala Glu His Val Val Leu Ala Gly Arg Arg Gly
1170 1175 1180

Gly Gly Val Val Gly Ala Val Glu Leu Glu Arg Glu Leu Val Gly Leu
1185 1190 1195 1200

Gly Ala Lys Val Thr Phe Val Ser Cys Asp Val Gly Asp Arg Ala Ser
1205 1210 1215

Met Val Gly Leu Leu Gly Val Val Glu Gly Leu Gly Val Pro Leu Arg
1220 1225 1230

Gly Val Phe His Ala Ala Gly Val Ala Gln Val Ser Gly Leu Gly Glu
1235 1240 1245

Val Ser Leu Ala Glu Ala Gly Gly Val Leu Gly Gly Lys Ala Val Gly
1250 1255 1260

Ala Glu Leu Leu Asp Glu Leu Thr Ala Gly Val Glu Leu Asp Ala Phe
1265 1270 1275 1280

Val Leu Phe Ser Ser Gly Ala Gly Val Trp Gly Ser Gly Gly Gln Ser
1285 1290 1295

Val Tyr Ala Ala Ala Asn Ala His Leu Asp Ala Leu Ala Glu Arg Arg
1300 1305 1310

Arg Ala Gln Gly Arg Pro Ala Thr Ser Val Ala Trp Gly Leu Trp Gly
1315 1320 1325

Gly Glu Gly Met Gly Ala Asp Glu Gly Val Thr Glu Phe Tyr Ala Glu
1330 1335 1340

Arg Gly Leu Ala Pro Met Arg Pro Glu Ser Gly Ile Glu Ala Leu His
1345 1350 1355 1360

Thr Ala Leu Asn Glu Gly Asp Thr Cys Val Thr Val Ala Asp Ile Asp
1365 1370 1375

Trp Glu His Phe Val Thr Gly Phe Thr Ala Tyr Arg Pro Ser Pro Leu
1380 1385 1390

Ile Ser Asp Ile Pro Gln Val Arg Ala Leu Arg Thr Pro Glu Pro Thr
1395 1400 1405

Val Asp Ala Ser Asp Gly Leu Arg Arg Arg Val Asp Ala Ala Leu Thr
1410 1415 1420

Pro Arg Glu Arg Thr Lys Val Leu Val Asp Leu Val Arg Thr Val Ala
1425 1430 1435 1440

Ala Glu Val Leu Gly His Asp Gly Ile Gly Gly Ile Gly His Asp Val
1445 1450 1455

Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Ala Ala Val Arg Met Arg
1460 1465 1470

Gly Arg Leu Ala Glu Ala Thr Gly Leu Val Leu Pro Ala Thr Val Ile
1475 1480 1485

Phe Asp His Pro Thr Val Asp Arg Leu Gly Gly Ala Leu Leu Glu Arg
1490 1495 1500

Leu Ser Ala Asp Glu Pro Ala Pro Gly Gly Ala Pro Glu Pro Ala Gly
1505 1510 1515 1520

Gly Arg Pro Ala Thr Pro Pro Pro Ala Pro Glu Pro Ala Val His Asp
1525 1530 1535

Ala Asp Ile Asp Glu Leu Asp Ala Asp Ala Leu Ile Arg Leu Ala Thr
1540 1545 1550

Gly Thr Ala Gly Pro Ala Asp Gly Thr Pro Ala Asp Gly Gly Pro Asp
1555 1560 1565

Ala Ala Ala Thr Ala Pro Asp Gly Ala Pro Glu Gln
1570 1575 1580

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1891 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Met Ser Pro Ser Met Asp Glu Val Leu Gly Ala Leu Arg Thr Ser Val
1 5 10 15

Lys Glu Thr Glu Arg Leu Arg Arg His Asn Arg Glu Leu Leu Ala Gly
20 25 30

Ala His Glu Pro Val Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly
35 40 45

Gly Val Ser Thr Pro Asp Asp Leu Trp Glu Leu Ala Ala Asp Gly Val
50 55 60

Asp Ala Ile Thr Pro Phe Pro Ala Asp Arg Gly Trp Asp Glu Asp Ala
65 70 75 80

Val Tyr Ser Pro Asp Pro Asp Thr Pro Gly Thr Thr Tyr Cys Arg Glu
85 90 95

Gly Gly Phe Leu Thr Gly Ala Gly Asp Phe Asp Ala Ala Phe Phe Gly
100 105 110

Ile Ser Pro Asn Glu Ala Leu Val Met Asp Pro Gln Gln Arg Leu Leu

115 120 125

Leu Glu Thr Ser Trp Glu Thr Leu Glu Arg Ala Gly Ile Val Pro Ala
130 135 140

Ser Leu Arg Gly Ser Arg Thr Gly Val Phe Val Gly Ala Ala His Thr
145 150 155 160

Gly Tyr Val Thr Asp Thr Ala Arg Ala Pro Glu Gly Thr Glu Gly Tyr
165 170 175

Leu Leu Thr Gly Asn Ala Asp Ala Val Met Ser Gly Arg Ile Ala Tyr
180 185 190

Ser Leu Gly Leu Glu Gly Pro Ala Leu Thr Ile Gly Thr Ala Cys Ser
195 200 205

Ser Ser Leu Val Ala Leu His Leu Ala Val Gln Ser Leu Arg Arg Gly
210 215 220

Glu Cys Asp Leu Ala Leu Ala Gly Gly Val Ala Val Met Pro Asp Pro
225 230 235 240

Thr Val Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Val Asp Gly
245 250 255

Arg Cys Lys Ala Phe Ala Glu Gly Ala Asp Gly Thr Ala Trp Ala Glu
260 265 270

Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn
275 280 285

Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp
290 295 300

Gly Ala Ser Asn Gly Leu Thr Ala Pro Ser Gly Pro Ala Gln Gln Arg
305 310 315 320

Val Ile Arg Glu Ala Leu Ala Asp Ala Gly Leu Thr Pro Ala Asp Val
325 330 335

Asp Val Val Glu Ala His Gly Thr Gly Thr Ala Leu Gly Asp Pro Ile
340 345 350

Glu Ala Gly Ala Leu Leu Ala Thr Tyr Gly Arg Glu Arg Val Gly Asp
355 360 365

Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala
370 375 380

Ala Ala Gly Val Gly Gly Val Ile Lys Val Val Gln Ala Met Arg His
385 390 395 400

Gly Ser Leu Pro Arg Thr Leu His Val Asp Ala Pro Ser Ser Lys Val
405 410 415

Glu Trp Ala Ser Gly Ala Val Glu Leu Leu Thr Glu Gly Arg Ser Trp
420 425 430

Pro Arg Arg Val Glu Arg Val Arg Arg Ala Ala Val Ser Ala Phe Gly

435 440 445

Val Ser Gly Thr Asn Ala His Val Val Leu Glu Glu Ala Pro Val Glu
450 455 460

Ala Gly Ser Glu His Gly Asp Gly Pro Gly Pro Asp Arg Pro Asp Ala
465 470 475 480

Val Thr Gly Pro Leu Pro Trp Val Leu Ser Ala Arg Ser Arg Glu Ala
485 490 495

Leu Arg Gly Gln Ala Gly Arg Leu Ala Ala Leu Ala Arg Gln Gly Arg
500 505 510

Thr Glu Gly Thr Gly Gly Gly Ser Gly Leu Val Val Pro Ala Ala Asp
515 520 525

Ile Gly Tyr Ser Leu Ala Thr Thr Arg Glu Thr Leu Glu His Arg Ala
530 535 540

Val Ala Leu Val Gln Glu Asn Arg Thr Ala Gly Glu Asp Leu Ala Ala
545 550 555 560

Leu Ala Ala Gly Arg Thr Pro Glu Ser Val Val Thr Gly Val Ala Arg
565 570 575

Arg Gly Arg Gly Ile Ala Phe Leu Cys Ser Gly Gln Gly Ala Gln Arg
580 585 590

Leu Gly Ala Gly Arg Glu Leu Arg Gly Arg Phe Pro Val Phe Ala Asp
595 600 605

Ala Leu Asp Glu Ile Ala Ala Glu Phe Asp Ala His Leu Glu Arg Pro
610 615 620

Leu Leu Ser Val Met Phe Ala Glu Pro Ala Thr Pro Asp Ala Ala Leu
625 630 635 640

Leu Asp Arg Thr Asp Tyr Thr Gln Pro Ala Leu Phe Ala Val Glu Thr
645 650 655

Ala Leu Phe Arg Leu Leu Glu Ser Trp Gly Leu Val Pro Asp Val Leu
660 665 670

Val Gly His Ser Ile Gly Gly Leu Val Ala Ala His Val Ala Gly Val
675 680 685

Phe Ser Ala Ala Asp Ala Ala Arg Leu Val Ser Ala Arg Gly Arg Leu
690 695 700

Met Arg Ala Leu Pro Glu Gly Gly Ala Met Ala Ala Val Gln Ala Thr
705 710 715 720

Glu Arg Glu Ala Ala Ala Leu Glu Pro Val Ala Ala Gly Gly Ala Val
725 730 735

Val Ala Ala Val Asn Gly Pro Gln Ala Leu Val Leu Ser Gly Asp Glu
740 745 750

Ala Ala Val Leu Ala Ala Ala Gly Glu Leu Ala Ala Arg Gly Arg Arg

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            755                 760                 765

Thr Lys Arg Leu Arg Val Ser His Ala Phe His Ser Pro Arg Met Asp
    770                 775                 780

Ala Met Leu Ala Asp Phe Arg Ala Val Ala Asp Thr Val Asp Tyr His
785                 790                 795                 800

Ala Pro Arg Leu Pro Val Val Ser Glu Val Thr Gly Asp Leu Ala Asp
                805                 810                 815

Ala Ala Gln Leu Thr Asp Pro Gly Tyr Trp Thr Arg Gln Val Arg Gln
            820                 825                 830

Pro Val Arg Phe Ala Asp Ala Val Arg Thr Ala Ser Ala Arg Asp Ala
        835                 840                 845

Ala Thr Phe Ile Glu Leu Gly Pro Asp Ala Val Leu Cys Gly Met Ala
    850                 855                 860

Glu Glu Ser Leu Ala Ala Glu Ala Asp Val Val Phe Ala Pro Ala Leu
865                 870                 875                 880

Arg Arg Gly Arg Pro Glu Gly Asp Thr Val Leu Arg Ala Ala Ala Ser
                885                 890                 895

Ala Tyr Val Arg Gly Ala Gly Leu Asp Trp Ala Ala Leu Tyr Gly Gly
            900                 905                 910

Thr Gly Ala Arg Arg Thr Asp Leu Pro Thr Tyr Ala Phe Gln His Ser
        915                 920                 925

Arg Tyr Trp Leu Ala Pro Ala Ser Ala Ala Val Ala Pro Ala Thr Ala
    930                 935                 940

Ala Pro Ser Val Arg Ser Val Pro Glu Ala Glu Gln Asp Gly Ala Leu
945                 950                 955                 960

Trp Ala Ala Val His Ala Gly Asp Val Ala Ser Ala Ala Ala Arg Leu
                965                 970                 975
Gly Ala Asp Asp Ala Gly Ile Glu His Glu Leu Arg Ala Val Leu Pro
            980                 985                 990

His Leu Ala Ala Trp His Asp Arg Asp Arg Ala Thr Ala Arg Thr Ala
        995                 1000                1005

Gly Leu His Tyr Arg Val Thr Trp Gln Ala Ile Glu Ala Asp Ala Val
    1010                1015                1020

Arg Phe Ser Pro Ser Asp Arg Trp Leu Met Val Glu His Gly Gln His
1025                1030                1035                1040

Thr Glu Cys Ala Asp Ala Ala Glu Arg Ala Leu Arg Ala Ala Gly Ala
                1045                1050                1055

Glu Val Thr Arg Leu Val Trp Pro Leu Glu Gln His Thr Gly Ser Pro
            1060                1065                1070

Arg Thr Glu Thr Pro Asp Arg Gly Thr Leu Ala Ala Arg Leu Ala Glu
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1075 1080 1085

Leu Ala Arg Ser Pro Glu Gly Leu Ala Gly Val Leu Leu Leu Pro Asp
1090 1095 1100

Ser Gly Gly Ala Ala Val Ala Gly His Pro Gly Leu Asp Gln Gly Thr
1105 1110 1115 1120

Ala Ala Val Leu Leu Thr Ile Gln Ala Leu Thr Asp Ala Ala Val Arg
1125 1130 1135

Ala Pro Leu Trp Val Val Thr Arg Gly Ala Val Ala Val Gly Ser Gly
1140 1145 1150

Glu Val Pro Cys Ala Val Gly Ala Arg Val Trp Gly Leu Gly Arg Val
1155 1160 1165

Ala Ala Leu Glu Val Pro Val Gln Trp Gly Gly Leu Val Asp Val Ala
1170 1175 1180

Val Gly Ala Gly Val Arg Glu Trp Arg Arg Val Val Gly Val Val Ala
1185 1190 1195 1200

Gly Gly Gly Glu Asp Gln Val Ala Val Arg Gly Gly Gly Val Phe Gly
1205 1210 1215

Arg Arg Leu Val Gly Val Gly Val Arg Gly Gly Ser Gly Val Trp Arg
1220 1225 1230

Ala Arg Gly Cys Val Val Val Thr Gly Gly Leu Gly Gly Val Gly Gly
1235 1240 1245

His Val Ala Arg Trp Leu Ala Arg Ser Gly Ala Glu His Val Val Leu
1250 1255 1260

Ala Gly Arg Arg Gly Gly Gly Val Val Gly Ala Val Glu Leu Glu Arg
1265 1270 1275 1280

Glu Leu Val Gly Leu Gly Ala Lys Val Thr Phe Val Ser Cys Asp Val
1285 1290 1295

Gly Asp Arg Ala Ser Val Val Gly Leu Leu Gly Val Val Glu Gly Leu
1300 1305 1310

Gly Val Pro Leu Arg Gly Val Phe His Ala Ala Gly Val Ala Gln Val
1315 1320 1325

Ser Gly Leu Gly Glu Val Ser Leu Ala Glu Ala Gly Gly Val Leu Gly
1330 1335 1340

Gly Lys Ala Val Gly Ala Glu Leu Leu Asp Glu Leu Thr Ala Gly Val
1345 1350 1355 1360

Glu Leu Asp Ala Phe Val Leu Phe Ser Ser Gly Ala Gly Val Trp Gly
1365 1370 1375

Ser Gly Gly Gln Ser Val Tyr Ala Ala Ala Asn Ala His Leu Asp Ala
1380 1385 1390

Leu Ala Glu Arg Arg Arg Ala Gln Gly Arg Pro Ala Thr Ser Val Ala

1395 1400 1405

Trp Gly Pro Trp Asp Gly Asp Gly Met Gly Glu Met Ala Pro Glu Gly
1410 1415 1420

Tyr Phe Ala Arg His Gly Val Ala Pro Leu His Pro Glu Thr Ala Leu
1425 1430 1435 1440

Thr Ala Leu His Gln Ala Ile Asp Gly Gly Glu Ala Thr Val Thr Val
1445 1450 1455

Ala Asp Ile Asp Trp Glu Arg Phe Ala Pro Gly Phe Thr Ala Phe Arg
1460 1465 1470

Pro Ser Pro Leu Ile Ala Gly Ile Pro Ala Ala Arg Thr Ala Pro Ala
1475 1480 1485

Ala Gly Arg Pro Ala Glu Asp Thr Pro Thr Ala Pro Gly Leu Leu Arg
1490 1495 1500

Ala Arg Pro Glu Asp Arg Pro Arg Leu Ala Leu Asp Leu Val Leu Arg
1505 1510 1515 1520

His Val Ala Ala Val Leu Gly His Ser Glu Asp Ala Arg Val Asp Ala
1525 1530 1535

Arg Ala Pro Phe Arg Asp Leu Gly Phe Asp Ser Leu Ala Ala Val Arg
1540 1545 1550

Leu Arg Arg Arg Leu Ala Glu Asp Thr Gly Leu Asp Leu Pro Gly Thr
1555 1560 1565

Leu Val Phe Asp His Glu Asp Pro Thr Ala Leu Ala His His Leu Ala
1570 1575 1580

Gly Leu Ala Asp Ala Gly Thr Pro Gly Pro Gln Glu Gly Thr Ala Arg
1585 1590 1595 1600

Ala Glu Ser Gly Leu Phe Ala Ser Phe Arg Ala Ala Val Glu Gln Arg
1605 1610 1615

Arg Ser Ser Glu Val Val Glu Leu Met Ala Asp Leu Ala Ala Phe Arg
1620 1625 1630

Pro Ala Tyr Ser Arg Gln His Pro Gly Ser Gly Arg Pro Ala Pro Val
1635 1640 1645

Pro Leu Ala Thr Gly Pro Ala Thr Arg Pro Thr Leu Tyr Cys Cys Ala
1650 1655 1660

Gly Thr Ala Val Gly Ser Gly Pro Ala Glu Tyr Val Pro Phe Ala Glu
1665 1670 1675 1680
Gly Leu Arg Gly Val Arg Glu Thr Val Ala Leu Pro Leu Ser Gly Phe
1685 1690 1695

Gly Asp Pro Ala Glu Pro Met Pro Ala Ser Leu Asp Ala Leu Ile Glu
1700 1705 1710

Val Gln Ala Asp Val Leu Leu Glu His Thr Ala Gly Lys Pro Phe Ala

1715 1720 1725

Leu Ala Gly His Ser Ala Gly Ala Asn Ile Ala His Ala Leu Ala Ala
1730 1735 1740

Arg Leu Glu Glu Arg Gly Ser Gly Pro Ala Ala Val Val Leu Met Asp
1745 1750 1755 1760

Val Tyr Arg Pro Glu Asp Pro Gly Ala Met Gly Glu Trp Arg Asp Asp
1765 1770 1775

Leu Leu Ser Trp Ala Leu Glu Arg Ser Thr Val Pro Leu Glu Asp His
1780 1785 1790

Arg Leu Thr Ala Met Ala Gly Tyr Gln Arg Leu Val Leu Gly Thr Arg
1795 1800 1805

Leu Thr Ala Leu Glu Ala Pro Val Leu Leu Ala Arg Ala Ser Glu Pro
1810 1815 1820

Leu Cys Ala Trp Pro Pro Ala Gly Gly Ala Arg Gly Asp Trp Arg Ser
1825 1830 1835 1840

Gln Val Pro Phe Ala Arg Thr Val Ala Asp Val Pro Gly Asn His Phe
1845 1850 1855

Thr Met Leu Thr Glu His Ala Arg His Thr Ala Ser Leu Val His Glu
1860 1865 1870

Trp Leu Asp Ser Leu Pro His Gln Pro Gly Pro Ala Pro Leu Thr Gly
1875 1880 1885

Gly Lys His
1890

Claims

1. An isolated DNA molecule consisting of a nucleotide sequence that encodes a polypeptide wherein said polypeptide consists of a platenolide synthase domain.

2. The isolated DNA molecule of claim 1 wherein the nucleotide sequence is selected from the group consisting of: nucleotides 392 to 1603, 1922 to 2995, 3173 to 3424, 3527 to 4798, 5135 to 6208, 7043 to 7597, 7946 to 8197, 8270 to 9541, 9899 to 10909, 10985 to 11530, 12596 to 13153, 13469 to 13720, 14148 to 15422, 15789 to 16844, 16914 to 17510, 18612 to 19166, 19479 to 19730, 20215 to 21486, 21889 to 22872, 23638 to 24159, 24484 to 24678, 24742 to 26016, 26371 to 27381, 27442 to 27966, 28843 to 29892, 29905 to 30462, 30760 to 31002, 31428 to 32696, 33024 to 34022, 34770 to 35327, 35586 to 35837, 36257 to 37528, 37898 to 38905, 39851 to 40408, 40658 to 40909, and 41297 to 41395 all in SEQ ID NO: 1.

3. A polypeptide consisting of an amino acid sequence wherein said polypeptide consists of a platenolide synthase domain.

4. A polypeptide of claim 3 wherein the amino acid sequence is selected from the group consisting of:

(a) amino acids 15 to 418, 525 to 882, 942 to 1025, 1060 to 1483, 1596 to 1953, 2232 to 2416, 2533 to 2616, 2641 to 3064, 3184 to 3520, 3546 to 3727, 4083 to 4268, and 4374 to 4457 all in SEQ ID NO: 2;
(b) amino acids 35 to 459, 582 to 933, 957 to 1155, 1523 to 1707, and 1812 to 1895 all in SEQ ID NO: 3;
(c) amino acids 36 to 459, 594 to 921, 1177 to 1350, 1459 to 1523, 1545 to 1969, 2088 to 2424, 2445 to 2619, 2912 to 3261, 3266 to 3451, and 3551 to 3631 all in SEQ ID NO: 4;

(d) amino acids 34 to 456, 566 to 898, 1148 to 1333, and 1420 to 1503 all in SEQ ID NO: 5; and
(e) amino acids 35 to 458, 582 to 917, 1233 to 1418, 1502 to 1585, 1715 to 1747 all in SEQ ID NO: 6.

5. The isolated DNA molecule of claim 1 wherein the nucleotide sequence is selected from the group consisting of: nucleotides 392 to 3424, 3527 to 8197, 8270 to 13720, 14148 to 19730, 20215 to 24678, 24742 to 31002, 31428 to 35837, and 36257 to 41395 all in SEQ ID NO: 1.

6. A polypeptide of claim 3 wherein the amino acid sequence is selected from the group consisting of:

(a) amino acids 15 to 1025, 1060 to 2616, and 2641 to 4457 all in SEQ ID NO: 2;
(b) amino acids 35 to 1895 in SEQ ID NO: 3;
(c) amino acids 36 to 1523, and 1545 to 3631 all in SEQ ID NO: 4;
(d) amino acids 34 to 1503 in SEQ ID NO: 5; and
(e) amino acids 35 to 1747 in SEQ ID NO: 6.

7. The isolated DNA molecule of claim 1 wherein the nucleotide sequence is selected from the group consisting of: nucleotides 350 to 14002, 14046 to 20036, 20110 to 31284, 31329 to 36071, and 36155 to 41830 all in SEQ ID NO: 1.

8. A homogenous preparation of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, and 6.

9. An isolated DNA molecule consisting of nucleotide sequence of SEQ ID NO: 1

10. A recombinant DNA vector comprising the DNA molecule of claim 1.

11. A recombinant DNA vector comprising the DNA molecule of claim 2.

12. A recombinant DNA vector comprising the DNA molecule of claim 5.

13. A recombinant DNA vector comprising the DNA molecule of claim 7.

14. A recombinant DNA vector comprising the DNA molecule of claim 9.

15. A host cell transformed with a recombinant DNA vector of Claim 10.

16. A host cell transformed with a recombinant DNA vector of Claim 11.

17. A host cell transformed with a recombinant DNA vector of Claim 12.

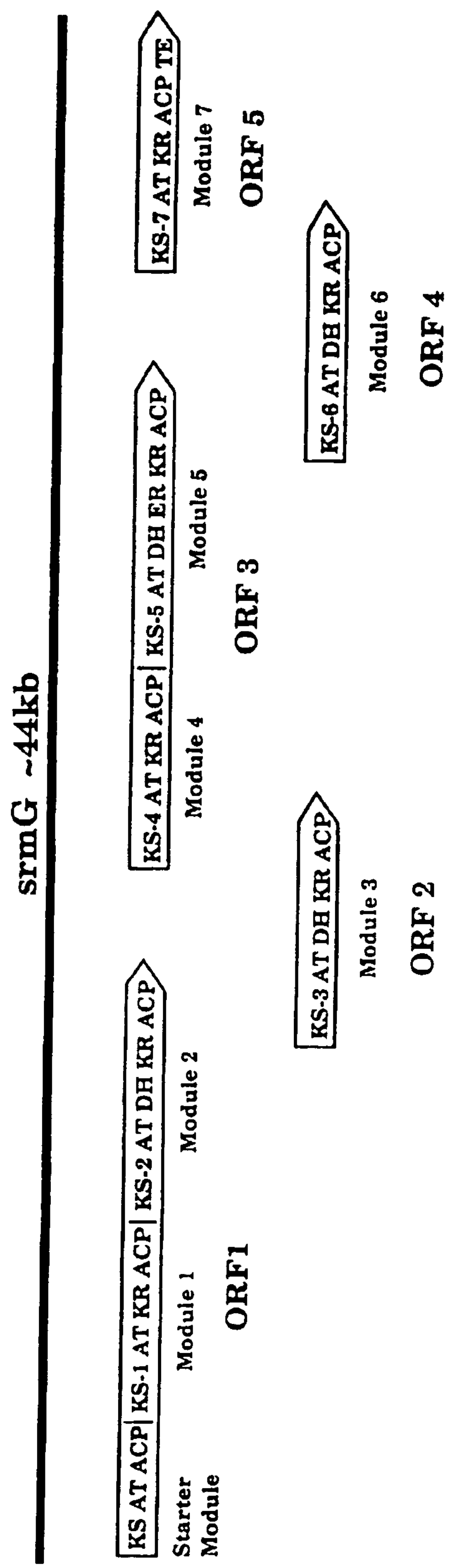
18. A host cell transformed with a recombinant DNA vector of Claim 13.

19. A host cell transformed with a recombinant DNA vector of Claim 14.

20. The recombinant DNA vector deposited under accession number NRRL B-21500.

21. The recombinant DNA vector deposited under accession number NRRL B-21499.

Fig. 1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KS-2 AT DH KR ACP
Starter Module
Module 1
Module 2
ORF1
KS-3 AT DH KR ACP
Module 3
ORF 2
KS-4 AT KR ACP
KS-5 AT DH ER KR ACP
Module 4
Module 5
ORF 3
KS-6 AT DH KR ACP
Module 6
ORF 4
KS-7 AT KR ACP TE
Module 7
ORF 5

Fig. 2

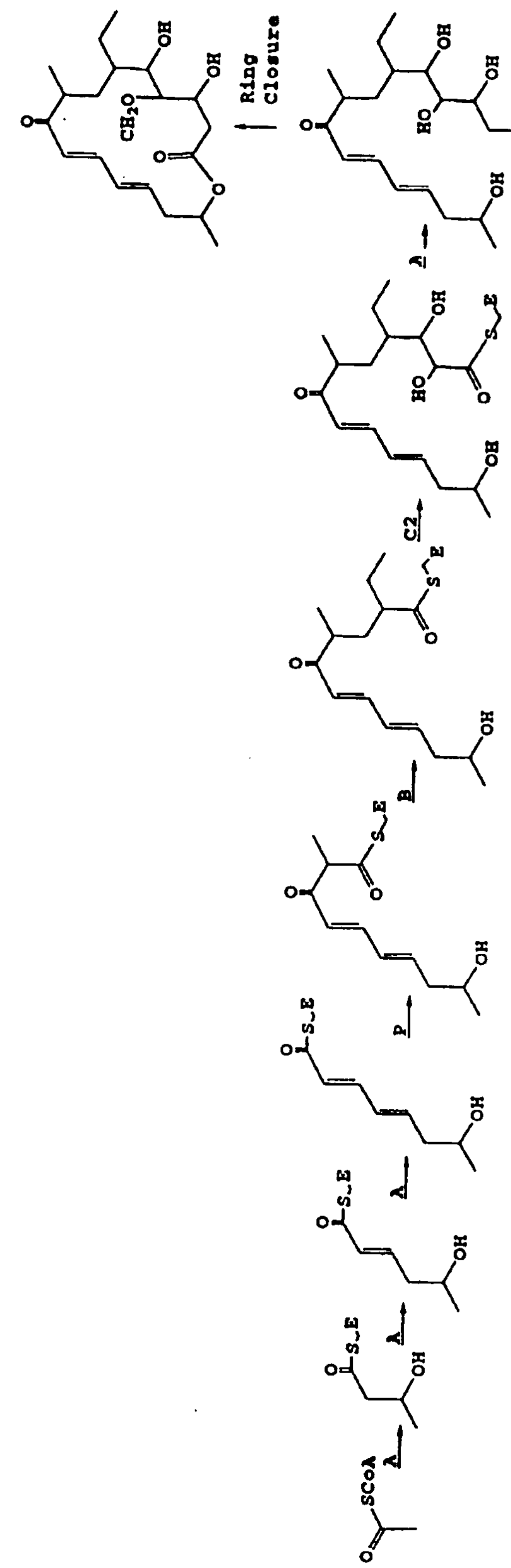
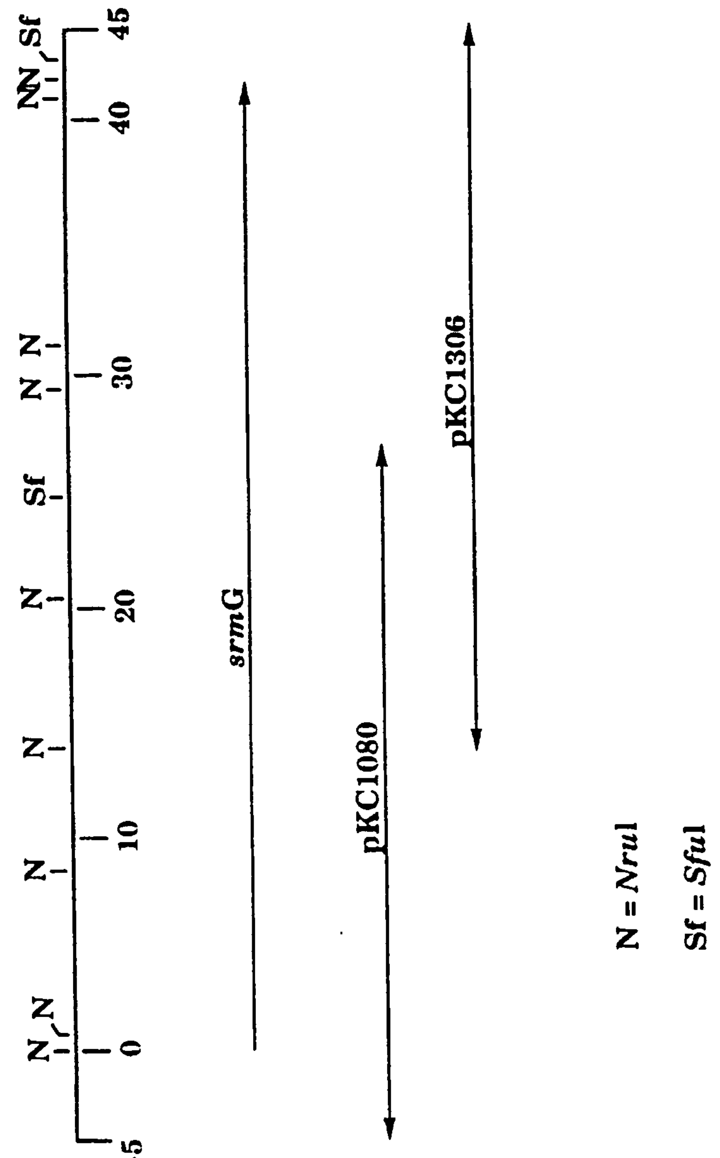


Fig. 3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N = NruI
Sf = SfuI